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13. ABSTRACT (Maximum 200 Words)

Accumulating evidence indicates that the "biobehavioral model" of health and disease may have considerable relevance for cancer generally, and breast cancer in particular. Broadly stated, this model proposes that what people think and feel affects the state of their health in two basic ways: by affecting their behavioral choices (e.g., smoking) and by affecting biological processes (e.g., cortisol levels) that affect risk and response to disease. Given the complexity of the interactions postulated by the biobehavioral model, to fully explore its implications for breast cancer it will be important to increase the number of researchers with the broad-based training that allows them to conduct truly interdisciplinary research addressing issues that transcend traditional disciplinary boundaries. Our Post-doctoral Training Program in Biobehavioral Breast Cancer Research was designed to provide trainees with advanced degrees in relevant areas (e.g., epidemiology, medicine, psychology, public health) with the necessary intellectual background needed to "speak the language" of the multiple relevant disciplines and with the "hands-on" experience under the tutelage of experienced mentors necessary to do interdisciplinary research and become independent investigators. Trainees have demonstrated proficiency in doing research and reporting results.

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5. INTRODUCTION:

Despite encouraging news that cancer incidence and mortality rates inched downward in the last decade of the 20th century, breast cancer continues to be a preeminent cause of morbidity and mortality among American women. Growing evidence indicates that the "biobehavioral model" of health and disease may have considerable relevance for cancer generally, and breast cancer in particular. Broadly stated, the Biobehavioral model proposes that what people think and feel affects the state of their health in two fundamental ways: by affecting their behavioral choices (e.g., consumption of alcoholic beverages) and /or by affecting biological processes (e.g., immune defenses) that may affect risk of disease and prognosis. Biobehavioral interactions have received increasing attention in breast cancer research over recent years. Through their effects on behavioral choices, cognitive and emotional factors are now recognized to influence women's risk of developing breast cancer, compliance with screening guidelines, interest and uptake in genetic testing, response to treatment, as well as contribute to quality of life among breast cancer survivors. Although there is some evidence that psychosocial interventions may affect survival, the impact of cognitive and emotional effects on biological processes involved in breast cancer incidence, progression, or recurrence has yet to be elucidated. Effects of cognitive and emotional factors on treatment related side effects are increasingly well documented, however. Perhaps reflecting the dearth of investigators with broad-based interdisciplinary training in this area, few studies have explored the possibility that interactions among psychological factors, behavioral choices, and biology may have important implications for breast cancer (e.g., the risk of developing breast cancer may be particularly high among women who have high levels of stress in conjunction with exposure to environmental toxins).

The importance of promoting broad-based research efforts on biopsychosocial and behavioral factors in all aspects of cancer (prevention, detection, diagnosis, treatment, and long term survival) has recently been emphasized in reports prepared by two blue ribbon panels for the National Cancer Institute. These reports have underscored the need for an expanded emphasis on research examining basic behavioral, psychological and social processes, aimed at increasing our understanding of the mechanisms underlying behavioral change (e.g., alcohol consumption) from the individual level (e.g., perceptions of risk) to the group (e.g., family influences) and society (e.g., social class) levels. In addition, the need for new initiatives in biopsychosocial research to explore interactions among biological, psychological, and social processes in cancer etiology, progression and response to treatment, was also emphasized. These reports have further noted the critical need to develop a cadre of highly trained research scientists with the necessary interdisciplinary skills to effectively and efficiently address these complex issues.

Our Postdoctoral Training Program in Biobehavioral Breast Cancer Research was designed to provide trainees with advanced degrees in relevant areas (e.g., epidemiology, medicine, psychology, public health) with the necessary intellectual background needed to "speak the languages" of the multiple relevant disciplines and with the "hands-on" experience under the tutelage of experienced mentors necessary to do interdisciplinary research and become independent investigators in this underdeveloped area of research.

6. BODY:

6.1 OVERVIEW: During the past year of a first no-cost extension of this Postdoctoral Training Program in Biobehavioral Breast Cancer Research our primary focus has been the continued implementation and continued improvement of all aspects of the training program for the Trainees previously recruited to the Program (see below). A secondary goal was to husband some of the funds on this grant with the intention of recruiting a Trainee to focus their hands-on research work with us on one of the three projects supported by our Army Behavioral Center of Excellence, "Genetic Factors in Breast Cancer: Center for Interdisciplinary Biobehavioral Research" as specified in that proposal (DAMD-17-01-1-0334). Although funded, initiation of those research projects has been delayed, as we have been awaiting approval by the Army IRB. We have therefore not been able to initiate the recruitment process for a Trainee to work on any of the projects until recently, when one of the three projects (Project 1: Behavior, Estrogen Metabolism, and Breast Cancer Risk: A Molecular Epidemiologic Study, Principal Investigator, Dr. Christine Ambrosone) did receive Army IRB approval. We have therefore formally requested, and have been awarded, a second no-cost extension to provide support for one new trainee, who will be recruited specifically to focus their research on that project over the next year.

6.2. DETAILED DESCRIPTON OF PROGRESS (Task 3 a-k):

a) Consistent with our proposed program of work, we did not advertise, nor recruit new applicants. We have nonetheless continued to receive applications from strong candidates around the country, as well as from abroad.

b) During the past year of no-cost extension we have not recruited any new trainees.

c) We have conducted a series of Core Course lectures presented by members of the faculty of the Mount Sinai School of Medicine, supplemented by outside speakers with particular expertise on relevant topics. For example, internal speakers have included: Dr. Christine Ambrosone, who provided an integrated series of three lectures on grant writing in Cancer Prevention and Control.

d) In addition we have supported a series of research seminars by Mount Sinai faculty and outside speakers to provide Trainees with exposure to recent developments in Biobehavioral Medicine, as well as related disciplines. A recent outside speaker (4/30/2004) was Dr. Camille Wortman from SUNY at Stonybrook, who gave a seminar on "Variability in Responses to the Loss of a Loved One: Cultural Understanding vs. Scientific Evidence."

e) Many of the outside speakers have also graciously agreed to do an additional informal Career Development Seminar for Trainees over lunch on the day of their research seminar presentation. As indicated above, both the Core Course Curriculum and Seminar Series have been running over the past year.

f) We continue to emphasize the hands-on portion of the training program through the active mentoring of trainees by federally-funded faculty members.

g) The Luncheon Lecture series (sometimes rescheduled as the "Bagel Breakfast" meeting), covering recent journal articles, works in progress by local investigators, and career development considerations by outside speakers has been scheduled and run.

h) Guidance in the development of independent research projects has been provided by the mentors for each Trainee, as well as by feedback from other members of the faculty made more informally as part of the Luncheon Lecture series.

i) Oversight for each Trainee's independent project is being provided by their Mentor and more informally by the rest of the faculty at Work-in-Progress (WIP) presentations as part of the Luncheon Lecture series.

j) Formal evaluations of Trainees and the Program have been conducted (e.g., at the end of each Trainee's first year of the Program).

k) In the first year of each Trainee's participation in the program, the focus has been on preparation of research reports from previous relevant research they may have conducted before joining the program, the preparation of research reports from the data collected from projects previously collected by their Mentors, and the preparation of initial reports concerning data which they collected during their first year of the Program. The development of Trainee's skills in grant writing has been fostered by a formal mini-series of lectures on grant writing; by one-on-one tutorials about the process as their Mentors have written and submitted grants; and by participation in our in-house grant review meetings in which faculty present their preliminary drafts of applications.

6.3 BRIEF DESCRIPTION OF CURRENT TRAINEES AND THEIR ACTIVITIES:

DR. ANNE FATONE: Dr. Fatone received a Ph.D. in Clinical & Health Psychology from Yeshiva University in New York, NY. Her research has focused on the effects of psychosocial factors in participation of medical minority populations in cancer prevention efforts. Most of her work has involved residents of East Harlem, NYC and has been conducted through our NCI funded East Harlem Partnership for Cancer Awareness. Dr. Fatone has accepted a position as an Instructor at the Mount Sinai School of Medicine.

DR. MARIA KANGAS: Dr. Kangas received a Ph.D. in Psychology from the University of New South Wales, Australia. Her research has focused on post traumatic stress disorder and the theoretical and empirical implications of considering cancer and its treatment to be a traumatic event. Dr. Kangas has recently accepted a position as an Assistant Professor at Macquarie University in Sydney Australia.

DR. NAA OYO KWATE: Dr. Kwate received a Ph.D. in Clinical Psychology from St. John's University in New York. Her research has focused on health disparities in cancer prevention and control. In one recent paper (see below), she reported that the experience of racism in African American women is associated with increased health risks. Dr. Kwate has applied for a number of positions and anticipates an academic career involving teaching and research.

DR. KRISTIN TATROW: Dr. Tatrow received a Ph.D. in Clinical Psychology from The State University of New York – Albany. Her research has focused on psychological aspects of pain due to various conditions in women. She is also interested in the investigation of the effectiveness of cognitive-behavior therapy for reducing pain and psychological distress in breast cancer patients. In one recent paper (see below), she reported that patients with higher activity levels had less distress prior to breast surgery for cancer. Dr. Tatrow has applied for a number of academic positions and anticipates a career involving university teaching and research.

6.3 BRIEF DESCRIPTION OF PAST TRAINEES AND THEIR CURRENT ACTIVITIES:

DR. JULIE BRITTON: Dr. Britton received a Ph.D. in Epidemiology from Columbia University, in New York City. Her primary research interest has been the role energy balance (diet, physical activity and body size) in relation to breast cancer risk. She was recently awarded an NIH Academic Career Award (K07) to support her career development in this area of research. Dr. Britton is currently a Research Assistant Professor in the Department of Community Medicine at the Mount Sinai School of Medicine in New York City.

DR. DANIEL DAVID: Dr. David received a Ph.D. in Psychology from Babes-Bolyai University, Cluj-Napoca, Romania. His primary research interest has been the theoretical and empirical implications of cognitive-behavioral therapy with a particular interest in Rational Emotive-Behavior Therapy (REBT) and its application to clinical populations, including breast cancer patients. Dr. David is currently an Assistant Professor in the Department of Psychology at Babes-Bolyai University, Cluj-Napoca, Romania.

DR. JENNIFER EGERT: Dr. Egert received a Ph.D. in clinical psychology from Duke University, Durham, North Carolina. Her primary research interest has been the psychological impact of life threatening illness, including breast cancer. Dr. Egert is currently a Clinical Health Psychologist at the Veterans Administration New York Harbor Healthcare System in New York City.

DR. JOSEPHINE GUEVARRA: Dr. Guevarra received a Ph.D. in psychology from the City University of New York, New York. NY. Her primary research interest has been the impact of cultural and racial factors on psychological adjustment and screening behavior among women with family histories of breast cancer. Dr. Guevarra is currently a Program Manager, Sales and Distribution Market Intelligence at IBM in New York.

DR. YOUNGMEE KIM: Dr. Kim received a Ph.D. in Social Psychology from the University of Rochester, Rochester, NY. Her primary research interest has been the influence of family relationships on health and disease, including breast cancer. Dr. Kim is currently the Director of Family Studies, at the Behavioral Research Center of the American Cancer Society in Atlanta, Georgia.

DR. TRICIA TANG: Dr. Tang received a Ph.D. in Clinical Psychology from the University of Vermont. Her primary research interest has been the influence of cultural factors on cancer prevention and control in underserved communities. Dr. Tang is currently the Director of the Multiculturalism and Health Program and an Assistant Professor in the Department of Medical Education at the University of Michigan Medical School.

7. KEY RESEARCH ACCOMPLISHMENTS:

Conducted training program for 4 Postdoctoral Trainees
- Recruited trainee applications
- Evaluated potential trainees
- Developed and scheduled Core Curriculum
- Scheduled Seminar Series
- Ran Core Curriculum and Seminar Series
- Established "hands-on" research experience for each Trainee

Scheduled and ran Luncheon Lecture series
Guided development of independent research projects for each Trainee
Provided oversight for each Trainee's independent project
Conducted formal evaluations of Trainee and Program
Facilitated preparation of research reports and grant applications

8. REPORTABLE OUTCOMES:

Trainees in the Program over the annual reporting period are listed first, followed by matriculated Trainees previously in the Program.

8.1 TRAINEES IN THE PROGRAM DURING THE ANNUAL REPORTING PERIOD:

DR. ANNE FATONE – POSTERS, PRESENTATIONS, ABSTRACTS AND PAPERS:

Thompson, H., Wahl, E., Fatone, A., Brown, K., Kwate, N., Valdimarsdottir, H. (in press). Enhancing the readability of materials on genetic risk for breast cancer. Cancer Control.

Fatone, A., Jandorf, L., Modibo Baker, J., Brenner, B., Butts, G., Cornbill, R., Itzkowitz, S.H., Levin, M., Rothenberg, A., Sacks, H., Weeks, M., Redd, W.H. (submitted). East Harlem Partnership for Cancer Awareness (EHPCA): collaborative cancer screening and prevention research in an urban minority community.

Fatone, A., Moadel, A., Foley, F., Fleming, M. Jandorf, L. (2003). Urban Voices: A qualitative analysis of quality of life issues as described by women of color who are breast cancer survivors. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Salt Lake City Utah.

DR. MARIA KANGAS – POSTERS, PRESENTATIONS, ABSTRACTS AND PAPERS:

Kangas, M., & Tate, R.L. (submitted) Clumsiness, more than just a slip of the hands: the significance of clumsy gestures in apraxia following a left hemisphere stroke. Neuropsychological Rehabilitation.

Kangas, M., & Bryant, R. A. (submitted). Correlates of acute stress disorder in cancer patients. Journal of Traumatic Stress. (Revised and re-submitted March, 2003)

Kangas, M., Henry, J.L., & Bryant, R.A. (submitted). The relationship between acute stress disorder and posttraumatic stress disorder following cancer. Journal of Consulting and Clinical Psychology. (Revised and re-submitted March, 2003).

Kangas, M., Henry, J.L. & Bryant, R.A. (submitted). Predictors of posttraumatic stress disorder following cancer. Health Psychology.

Kangas, M. (2003). Acute Stress Disorder and Posttraumatic Stress Disorder Following Cancer. Presentation, Ruttenberg Cancer Centre, Mount Sinai Hospital, New York.

Kangas, M. (2003). Autobiographical memory functioning in cancer. Presentation, Ruttenberg Cancer Center, Mount Sinai Hospital, New York.

Kangas, M., & Bryant, R.A. (2003). Acute Stress Disorder (ASD) and PTSD Following Head, Neck and Lung Cancer. Paper presented at the 37th Annual convention for the Association for Advancement of Behavior Therapy (AABT), Boston, U.S.A.

DR. NAA OYO KWATE – POSTERS, PRESENTATIONS, ABSTRACTS AND PAPERS:

Kwate NO, Valdimarsdottir HB, Guevarra JS, Bovbjerg DH Experiences of racist events are associated with negative health consequences for African American women. J Natl Med Assoc. 2003 Jun;95(6):450-60.

Kwate, N.O. The projection of Eurocentrism in projective testing. In: African-centered Psychology: Culture-focusing for multicultural competence. 2003. D.A. Azibo, (Ed.).Durham: Carolina Academic Press.

Kwate, N.O. (in press). The projection of eurocentrism in projective testing. African-centered Psychology. North Carolina Press.

Kwate, N.O. (in press). Cross-Validation of the Africentrism Scale. The Journal of Black Psychology.

Guevarra, J.S., Kwate, N.O., Tang, T.S., Valdimarsdottir, H.B., Freeman, H.P., & Bovbjerg, D.H. (in press). Acculturation and its relationship to smoking and breast self-examination frequency in African American women. Journal of Behavioral Medicine.

Kwate, N.O. African-centered psychology as a heretical challenge to North American mental health.

Kwate, N.O. Neo-colonialism, neo-minstrelsy, and neoplasms: Or, do racism and cultural identity affect African American health? (Invited lecture). Integrative and Behavioral Cardiology, Mount Sinai School of Medicine, 2003.

Kwate, N.O.A., Valdimarsdottir, H.B., Bovbjerg. D.H. Ethnic differences in etiological attributions for breast cancer among healthy African American and European American women. (Citation Paper). The Annual Meeting of the Society of Behavioral Medicine, Salt Lake City, Utah (2003).

DR. KRISTIN TATROW – POSTERS, PRESENTATIONS, ABSTRACTS AND PAPERS:

Tatrow, K., Blanchard, E. B., & Silverman, D. J. Post-traumatic headache: An exploratory treatment study. Applied Psychophysiol Biofeedback. 2003; Dec 28(4); 267-78.

Tatrow, K., Blanchard, E. B., Hickling, E. J., & Silverman, D. J. Post-traumatic headache: Biopsychosocial comparisons to multiple controls. Headache. 2003 Jul-Aug;43(7); 755-766.

Tatrow, K., & Blanchard, E. B. (in press). Menstrual cycle effects on headache activity of tension-type headache: Preliminary data.

Tatrow, K., Montgomery, G. H., Avellino, M., & Bovbjerg, D. H. (in press). Activity and sleep contribute to levels of anticipatory distress in breast surgery patients. Behavioral Medicine.

Tatrow, K., Montgomery, G. H., Erlich, M. D., Avellino, M. D., Birk, J. S., & Bovbjerg, D. H. (2003). The impact of surgery and family histories of breast cancer on distress. In K. Tatrow (Chair), Recent findings in cancer research. Symposium at the annual meeting of the American Psychological Association, Toronto, Ontario, CANADA.

Montgomery, G. H., Tatrow, K., David, D., Avellino, M. D., Birk, J. S., & Bovbjerg, D. H. (2003). Pre-surgery expectancies and distress predict side-effects of breast cancer surgery. In K. Tatrow (Chair), Recent findings in cancer research. Symposium at the annual meeting of the American Psychological Association, Toronto, Ontario, CANADA.

Avellino, M. D., Tatrow, K., Montgomery, G. H., & Bovbjerg, D. H. (2003). Exercise and sleep predict pre-surgical distress in breast surgery patients. Poster presented at the annual meeting of the American Psychological Association, Toronto, Ontario, CANADA.

8.2 MATRICULATED TRAINEES PREVIOUSLY IN THE PROGRAM:

DR. JULIE BRITTON (former trainee) – PAPERS:

Wolff, M.S., Britton, J.A., Wilson, V.P. Environmental risk factors for breast cancer among African-American women. Cancer. 2003;97(1 Suppl):289-310.

Teitelbaum SL, Britton JA, Gammon MD, Schoenberg JB, Brogan DJ, Coates RJ, Daling JR, Malone KE, Swanson CA, Brinton LA. Occupation and breast cancer in women 20 to 44 years of age. Cancer Causes and Control. 2003;14(7): 627-637.

Muscat JE, Britton JA, Djordjevic MV, Citron ML, Kemeny M, Busch-Devereaux E, Pittman B, Stellman SD. Adipose concentrations of organochlorine compounds and breast cancer recurrence in Long Island, New York. Cancer Epidemiology Biomarkers & Prevention 2003:12:1474-1478.

Britton JA, Wolff MS, Lapinski R, Forman J, Hochman S, Kabat GC, Godbold J, Larson S, Berkowitz GS. Characteristics of pubertal development in a multi-ethnic population of nine-year old girls. Annals of Epidemiology. 2004;Mar;14(3):179-87.

Terry MB, Gammon MD, Zhang FF, Tawfik H, Teitelbaum SL, Britton JA, Subbaramaiah K, Dannenberg AJ, Neugut AI. Association of frequency and duration of aspirin use and hormone receptor status with breast cancer risk. Journal of the American Medical Association. 2004;May 26;291(20):2433-40.

Gammon, M.D., Santella, R.M., Neugut, A,I,, Eng, S.M., Teitelbaum, S.L., Paykin, A., Levin, B., Terry, M.B., Young, T., Wang, Q., Britton, J.A., Wolff, M.S., Stellman, S.D., Hatch, M., Kabat, G.C., Senie, R., Garbowski, G., Maffeo, C., Montalvan, P., Berkowitz, G.S., Kemeny, M., Citron, M., Schmabel, F., Schuss, A., Hajdu, S., Vincguerra, V. (submitted). PAH-DNA adducts and the risk of breast cancer among women on Long Island.

Wolff, M.S., Berkowitz, G.S., Lapinski, R., Britton, J.A., Forman, J., Hochman, S., Kabat, G.C., Godbold, J., Larson, S. (submitted). Ethnic differences in onset of puberty and the influence of diet.

DR. DANIEL DAVID (former trainee) - PAPERS:

Montgomery, G.H., David, D., Goldfarb, A.B., Silverstein, J.H., Weltz, C,R., Birk, J.S., Bovbjerg, D.H. (2003). Sources of anticipatory distress among breast surgery patients. Journal of Behavioral Medicine 26:153-164.

David, D., Montgomery, G.H., Holdevici, I. (2003). Romanian norms for the Harvard Group Scale of Hypnotic Susceptibility, Form A. International Journal of Clinical and Experimental Hypnosis 51:51-56.

David, D., & Brown, R. (in press). Suggestibility and negative priming: Two replications studies. International Journal of Clinical and Experimental Hypnosis.

Montgomery, G.H., David, D., DiLorenzo, T., Erblich, J. (in press). Is hoping the same as expecting? Discrimination between hopes and response expectancies for nonvolitional outcomes. Personality and Individual Differences.

David D, Montgomery GH, Bovbjerg DH. (in press). An empirical investigation of Albert Ellis' binary model of distress. Journal of Clinical Psychology.

David, D., Moore, M., & Domuta, A. (in press). Romanian psychology on the international psychological scene: A preliminary critical and empirical approach. European Psychologist.

DR. JENNIFER EGERT (former trainee) - PAPERS:

Egert, J.R., Keefe, F.J., Winer, E., Rimer, B. (submitted). Coping and social support as predictors of positive dimensions of psychological well-being among women who completed treatment for early stage breast cancer.

Egert, J.R., Keefe, F,J., Winer, E., Rimer, B. (submitted). Re-defining a "Good adjustment" to cancer: psychological well-being, coping and social support following breast cancer treatment.

Egert, J.R., Winer, E., Smith, M.Y., Rimer, B., Winkel, G., Keefe, F.J. (submitted). Psychological well-being, distress and quality of life following treatment for early stage breast cancer.

Smith, M.Y., Egert, J.R., Winkel, G., Jacobson, J. (submitted). Post-traumatic stress disorder and pain symptoms in persons with HIV/AIDS: A prospective study.

DR. JOSEPHINE GUEVARRA (former trainee) - PAPERS:

Kwate NO, Valdimarsdottir HB, Guevarra JS, Bovbjerg DH Experiences of racist events are associated with negative health consequences for African American women. Journal of the National Medical Association. 2003 Jun;95(6):450-60.

Guevarra, J.S., Tang, T.S., Valdimarsdottir, H.B., Freeman, H.P., Kwate, N.O., & Bovbjerg, D.H. (in press). Acculturation and its relationship to smoking and breast self-examination frequency in African American women. Journal of Behavioral Medicine.

DR. YOUNGMEE KIM (former trainee) - PAPERS:

Kim, Y., & Morrow, G. R. Changes in family relationships affect the development of chemotherapy-related nausea symptoms. Support Care Cancer. 2003;11(3): 171-177.

Kim, Y., Valdimarsdottir, H.B., Bovbjerg, D.H. Family histories of breast cancer, coping styles and psychological adjustment. Journal of Behavioral Medicine. 2003;June 26(3); 225-243.

Kim, Y., Kasser, T., & Lee, H. (in press). Self-concept, aspiration, and well-being in Korea and the United States. Journal of Social Psychology.

Kim, Y., Deci, E. L., & Zuckerman, M. (in press). The self-regulation of withholding negative emotions: Development of a questionnaire. Educational and Psychological Measurement.

Kim Y, Seidlitz L. Ro Y, Evinger J.S., Duberstein PR. (submitted). Spirituality and affect: A lifecourse perspective.

Kim, Y., Duberstein, P. R., Sörensen, S. & Larson, M. R. (submitted). Depression in spouses of people with lung cancer: Effects of personality, social support, and caregiving burden.

Kim, Y., Valdimarsdottir, H. B., & Bovbjerg, D. H. (submitted). The moderating effects of coping on the psychological impact of having a family history of breast cancer.

Sheldon, K. M., Elliot, A. J., Ryan, R. M., Chirkov, V., Kim, Y., Wu, C. Demir M., & Sun Z. (submitted). Autonomy and collectivism: Complementary, not conflicting.

Kim, Y. (submitted). Specialized and fragmented cognitive concept on the self and romantic relationships.

Kim, Y. (submitted). Emotional and cognitive consequences of adult attachment: The mediating effect of the self.

Kim, Y., Sahler, O.J., Messauer, L., & Vattimo, C. (submitted). Parental adjustment in childhood cancer: Marital and occupational issues.

DR. TRICIA TANG (former trainee) - PAPERS:

Tang, T.S., Bozynski, M.E., Mitchell, J.M., Haftel, H.M., Vanston, S.A., Anderson, R.M. (2003). Are residents more comfortable than faculty members when addressing sociocultural diversity in medicine? Academic Medicine. 78(6): 629-633.

Guevarra, J.S., Kwate, N.O., Tang, T.S., Valdimarsdottir, H.B., Freeman, H.P., & Bovbjerg, D.H. (in press). Acculturation and its relationship to smoking and breast self-examination frequency in African American women. Journal of Behavioral Medicine.

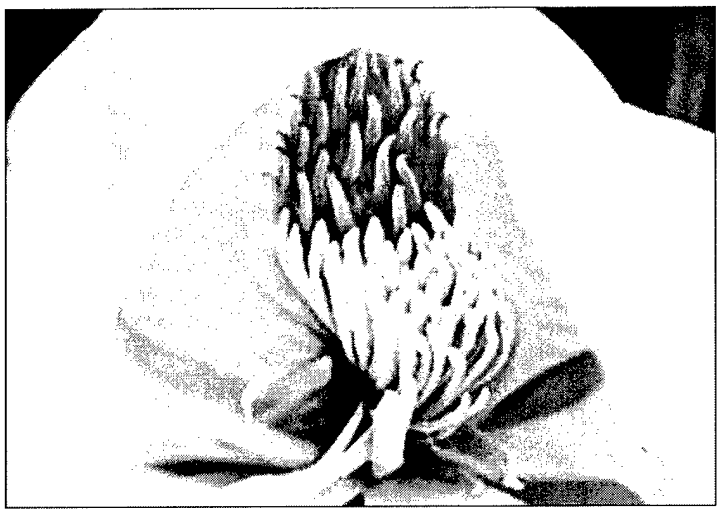
9. CONCLUSIONS:

During the past year, we have continued to successfully complete the Technical Objectives of the Postdoctoral Training Program in Biobehavioral Breast Cancer Research:

Aim 1. To provide postgraduate trainees a broad-based intellectual background needed to conduct interdisciplinary biobehavioral breast cancer research thorough structured didactic training (e.g., Core Curriculum Lecture Series, Advanced Seminars) and informal interactions with the Training Faculty and other active researchers.

Aim 2. To teach Trainees interdisciplinary research skills through hands-on participation in ongoing federally-funded breast cancer research programs of the Training Faculty and by having Trainees develop and conduct their own related biobehavioral research projects with the guidance of their research Mentors.

Aim 3. To foster the development of Trainees' independent research careers in biobehavioral breast cancer research through both formal instruction and direct experience with writing research papers and grants, under the direct tutelage of their Mentors.



Christine Zalewski. *Magnolia I.* Photograph.

Continued efforts are needed to create patient education materials that are easier to understand.

Enhancing the Readability of Materials on Genetic Risk for Breast Cancer

Hayley S. Thompson, PhD, Erica Wahl, MS, Anne Fatone, PhD, Karen Brown, MS, Naa Oyo A. Kwate, PhD, and Heiddis Valdimarsdottir, PhD

Background: *The number of individuals contemplating genetic testing is increasing, but the current materials and overall subject matter remain complex and not easily understood by many. The goal of this project was to evaluate efforts to revise and increase the readability of an existing information packet describing genetic risk for breast cancer.*

Methods: *Evaluation was conducted in two stages through two related studies. In Study 1, a focus group of multiethnic breast cancer survivors was assembled to obtain feedback on images included in the revised breast cancer genetics information packet. In Study 2, African American adult students in a literacy program evaluated the revised images (based on the feedback of the focus group in Study 1) and text of the information packet and provided ratings on readability, format, and appearance.*

Results: *Responses from Study 1 participants suggested that some of the images created for the packet needed to be clearer in the concepts they were intended to convey. In Study 2, ratings of adult learners suggested difficulty with word comprehension in spite of the inclusion of definitions and a glossary. The reading level achieved was markedly lower than the college reading level required by the original information packet and other patient-directed cancer genetics materials.*

Conclusions: *Although efforts to clarify written materials in order to better serve patients with low literacy received generally favorable responses, continued efforts to create more user-friendly patient education materials are warranted.*

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Introduction

Literacy is a critical yet often overlooked issue in the development and dissemination of printed cancer education materials. Results from the Department of Education National Adult Literacy Survey revealed that approximately 20% to 25% of the US adult population reads at or below a 5th-grade level and lacks the basic reading skills that would enable them to read and understand directions on a map or instructions on a medication.[1,2] Low reading comprehension is associated with lower recall of health-care information and lower satisfaction with the communication of such information.[1] It is not surprising, then, that low literacy levels are consistently associated with poorer health status.[3,4] Although the association between literacy level and cancer-related outcomes has not been examined specifically, reviews have revealed that most cancer education materials are written at a 10th-grade level or higher,[1] which would make such materials too difficult to understand for a significant portion of the population. Therefore, efforts to increase the readability of printed cancer-related information are necessary.

Little attention has also been paid to the literacy level required by materials developed for individuals at high risk for developing breast cancer due to their family history of the disease. It is estimated that 5% to 10% of breast cancer cases are due to mutations in two genes, *BRCA1* and *BRCA2*,[5,6] and testing to identify these mutations is now available commercially. In order to make an informed decision about testing, individuals should have some understanding of complex genetic information as well as the potential positive consequences of testing (eg, improved medical decision-making, increased information about relatives' cancer risk) and the negative consequences of testing (eg, increased worry about one's health status and the health of relatives, negative emotional reactions, and possible insurance or employment discrimination).[7-10] Richards and Ponder[11] assert that a general "genetic literacy" is a prerequisite for appropriate patient use of genetic tests. To date, there is no review of the readability of patient-directed cancer genetics materials in the literature. However, Gribble[12] investigated the readability of informed consent documents for *BRCA1/2* testing obtained from several research institutions. Such consent forms typically include a description of the genetic testing process, as well as the potential consequences of testing. Gribble reported that, on average, these documents were written at a grade level 1 year beyond high school graduation and had reading ease scores similar to those of academic journals. These results are indicative of what has been referred to as a "readability gap" between the language of cancer genetics materials and the reading skills of many people.[12]

The goal of the two studies presented here was to evaluate efforts to revise and increase the readability of an existing information packet describing genetic risk for breast cancer. These efforts were part of an ongoing research project at the Mount Sinai School of Medicine called Talking About Counseling and Testing (TACT). The primary aim of TACT is to evaluate the impact of culturally targeted genetic counseling vs standard genetic counseling on decisions to undergo *BRCA1/2* testing among African American breast cancer patients. As part of this aim, it was necessary to include supplementary printed materials that review the basic content of the counseling sessions. The readability of the information packet was an area of focus because, although the majority of low-level readers are white, people of color are more likely to perform at the lowest literacy levels.[13]

The current evaluation is unique in two ways. First, the revised information packet was reviewed by lay people who shared key characteristics with the packet's target audience: breast cancer survivors and adults with low literacy skills. Many readability evaluations of cancer education materials are based on objective scores and assessment tools (eg, the Flesch Reading Ease Formula, Flesch-Kincaid Grade Level Formula, the Readability Assessment Instrument, SMOG Readability Formula) that are used by or administered to professional-level reviewers.[14-17] Second, the current evaluation is unique in that it employed a two-stage approach: (1) Multiethnic breast cancer survivors, who met regularly as research subject recruiters for a separate study, participated in a focus group to provide feedback on images included as part of the revision. Members of this group of survivors were asked to participate due to their similarity to the information packet's target group in terms of breast cancer diagnosis and concerns about familial aspects of breast cancer risk. Their feedback was used to revise the images even further. (2) Next, ratings of both the revised images and text of the information packet were obtained from a class of African American adult learners with low literacy skills. These class members were included in our evaluation efforts because they not only shared the target group's ethnicity, but also were representative of the segment of the information packets' target group who are likely to demonstrate low reading comprehension according to national survey data. Both studies were components of educational efforts to increase awareness of genetic risk for breast cancer.

Study 1

Methods

In Study 1, a focus group of breast cancer survivors was organized to obtain feedback on images included in the revised breast cancer genetics information packet.

Participants

The focus group was composed of 7 women who were breast cancer survivors and who also served as Patient

Advocates for Research Participation (PARPs). These survivors recruit breast cancer patients for a separate, ongoing, large-scale case-control study at the Mount Sinai School of Medicine. The PARPs who participated in the current study were enlisted at a regular recruiter meeting and all attendees participated. Participants were 3 African American survivors, 3 white survivors, and 1 Latina survivor, ranging in age from 45 to 54 years. Of these women, 3 had completed high school and 4 had either an Associate's degree or a Bachelor's degree.

Materials and Measures

Participants were presented with the images included in a revised information packet describing genetic risk for breast cancer. The original information packet is part of a separate research study conducted at both the Lombardi Cancer Center at Georgetown University and Mount Sinai School of Medicine called Personal Aid to Health (PATH). The original information packet contains 26 pages of breast cancer genetics information followed by an additional 13 pages of resources. The information packet begins with an overview of the PATH study and provides background information on risk factors for breast and ovarian cancer. It then reviews the inheritance of cancer susceptibility, including a discussion of breast cancer susceptibility genes (specifically, *BRCA1* and *BRCA2*) and the cancer risks associated with alterations in these genes. The information packet also reviews the process of genetic testing and its benefits and limitations. Finally, the information packet includes a discussion of appropriate cancer screening and risk reduction options for breast cancer.

This information packet was revised for the TACT project because it was written at a considerably sophisticated level, the text was dense, and it had few pictures that facilitated comprehension of the text. This assessment is supported by a calculation of the packet's Flesch-Kincaid Grade Level, which is a function of the average length of sentences in a text and the average number of syllables per word. The Flesch-Kincaid Grade Level of the original packet was greater than grade 12. Readability was also assessed through the Flesch Readability Test, which determines reading ease and is based on a formula that yields a score of 0 (ie, extremely difficult to read, average sentence length is 37 words, average word is more than two syllables) to 100 (ie, very easy to read, average sentence length is 12 words, no words of more than two syllables). The original packet had a Flesch Reading Ease score of 39.5. As a score of 65 represents "plain English," a score of 39.5 suggests that the packet was written in fairly complex language.

Revision of Information Packet Text to Increase Readability — The existing information packet was revised using several strategies recommended for creating printed health-related materials appropriate for a wide range of reading levels.[1,18-20]

Word Substitution and Limiting of Sentence Length — The authors attempted to shorten sentences whenever possible. For example, the PATH heading, "Estimated Cancer Risks Associated with *BRCA1* and *BRCA2* Alterations" was revised as "What Does It Mean if I Have a *BRCA* Mutation?" Also, whenever possible, difficult words were substituted with simpler words. For example, the word *individual* was changed to *person*. However, in some instances, authors chose to retain an advanced word or term if it was commonly used by genetics professionals and there was no alternative word or term that was both succinct and conveyed the same meaning. Examples of such words or terms that were always defined but used repeatedly include *mutation*, *tamoxifen*, *chromosome*, and *variant*.

Comprehension of Difficult Words — All difficult words were presented in boldface type and defined in the text. They were also included in a glossary at the end of the information packet along with the pronunciation of the word and a more detailed definition.

Use of Analogies as Examples — Wherever possible, the authors used analogies that would be familiar to the information packet's target audience as a way of clarifying concepts.[20] One such example was the explanation of the meaning of specific *BRCA1/2* test results referred to as variants of uncertain significance. This type of result means that a genetic change was found but it is uncertain if this change has an effect on a person's risk for cancer. In certain cases, variant results can be further defined to indicate that the result is either likely or unlikely to be associated with an increased cancer risk. Such test results were explained in the revised information packet using the analogy of a commuter train ride, since this experience is familiar to the urban population from which the majority of participants would be recruited. In this analogy, readers were asked to imagine that they were taking an express train to make an appointment on Main Street. They were then asked to envision different scenarios that might occur during the ride that could each affect whether the rider will make it to the Main Street appointment on time. The likelihood of whether a rider will be on time for their appointment is related to the different types of variant results. For example, a scenario in which the train changes its route and the rider will probably not be on time is related to a variant result.

Other strategies applied to increase readability included the use of large font, use of headings to introduce new ideas, limited use of tables and graphs, and increased use of white space on a page[1,18-20] After this first revision, the readability of the information packet, which was 23 pages long, was significantly improved with a Flesch Reading Ease score of 63.7 and a Flesch-Kincaid Grade Level of 8.0. Although the packet was still above a 5th-grade reading level, readability scores may have been inflated by the retention of genetic and other medical terms that were multisyllabic. In fact, in exploratory analyses, the deletion

of all genetic terms alone improved readability somewhat (Flesch Reading Ease score = 68, Flesch-Kincaid Grade Level = 7.3). Therefore, it is possible that the information packet may have been easier to read than scores indicated. It was unclear whether the genetic and medical terms would present a significant obstacle to comprehension since all these terms were defined.

Revision of Information Packet Images — As part of the revision, we limited the use of tables and graphs and increased the number of pictures that accompanied different sections of the information packet as has been recommended to increase readability. Most of these images were cartoons created by a coauthor (N.O.K.). These cartoons accompanied specific text and demonstrated various genetic concepts. The original information packet included three tables and four pictures. The revised information packet included 10 pictures and one simple graph showing how breast cancer risk increases with age.

Procedures

A rapid focus group was moderated by two coauthors: a certified genetic counselor (K.B.) and a clinical psychologist (H.S.T.). Rapid focus group strategies are detailed by Krueger.[21] A rapid focus group is one adapted to accommodate emerging situations or immediate opportunities and is conducted when there is a need to collect and analyze data quickly.[21] In this instance, the immediate opportunity was a scheduled monthly meeting of the PARP recruiters. Additionally, there was a need to obtain feedback on images quickly in order to continue with evaluations of the complete information packet (images plus text). Rapid focus groups differ from standard focus groups in that they often "piggyback" on existing meetings or conferences and ask questions that are specific and limited in scope. Also, only approximately half of the questions of a standard focus group are used (4 to 7 questions vs approximately 12 questions).

First, the moderators introduced themselves and presented the primary objectives of the TACT project. Next, the objective of the rapid focus group was presented. Participants were informed that an information packet describing genetic risk for breast and ovarian cancer was being revised and specific feedback on the information packet's images was desired. Participants were told that because the information packet was intended for breast cancer patients, their opinions as breast cancer survivors were desired. For the purposes of the rapid focus group, we selected 5 of the 10 images that were best representative of the style of all cartoons. Three of these cartoons were presented with the original image they replaced, so that a total of 8 images were presented to the rapid focus group.

The original information packet included a photographic reproduction of chromosomal pairs (Fig 1). A cartoon (Fig 2), developed to replace Fig 1, depicted a pair of chromosomes that were anthropomorphized by giving them eyes, mouths, and arms. Fig 3 was a new image created for the revised information packet that described how chromosomes are inherited from parent to child. Fig 4 was also a new image created for the revised information packet to demonstrate the concept of genetic dominance. In this cartoon, one anthropomorphized mutated gene appeared to dominate a conversation with a normal gene. The mutated gene had a hand placed over the mouth of the normal gene, which had annoyed expression on its face. The original information packet also included an image showing the location of the *BRCA1* and *BRCA2* genes on the chromosomes (Fig 5). Fig 6, developed to replace Fig 5, was a cartoon of a gene living on a chromosome. Fig 7, from the original information packet, and Fig 8, a cartoon developed to replace Fig 7, both demonstrated dominant inheritance of a cancer susceptibility gene.

The images were displayed with an overhead projector. As each image was displayed, a brief explanation of the image was provided by the genetic counselor. Participants

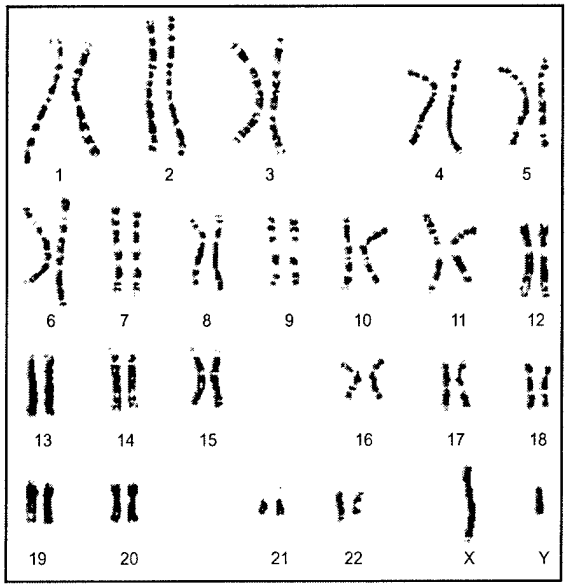

Fig 1. — Photographic reproduction of chromosomal pairs from the original information packet. Courtesy of Brynn Levy, PhD, at Mt. Sinai Medical Center, New York, NY.

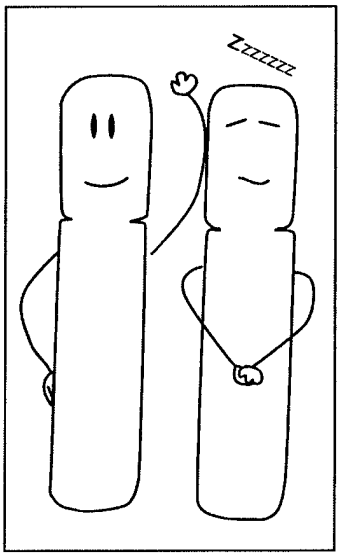

Fig 2. — A cartoon of a pair of chromosomes that were anthropomorphized by giving them eyes, mouths, and arms. This image was intended to replace Fig 1.

were asked (1) whether the image appeared consistent with the explanation provided, (2) their general opinions about how effective the cartoons were in helping to explain concepts, and (3) how appropriate the cartoons were for inclusion in the information packet. This last issue was important because researchers have recommended that developers of print materials use adult-looking visuals and recommend caution in using visuals that may make the materials appear less credible to an adult.[20] A notetaker (A.F.) was present to record responses. Note-based analysis was conducted to identify themes across questions that were asked about each image.[22]

Results

The two primary themes that emerged based on participants' responses to the images were related to the appropriateness and clarity of the cartoons. First, the majority of participants responded favorably to the new cartoons. Of the 5 new cartoons presented, 3 were well-received (Figs 3, 4, and 8), with participants indicating that these cartoons enhanced comprehension of genetic concepts. For example, several participants indicated that the cartoon in which one mutated gene appeared to dominate a conversation with a normal gene (Fig 4) was a clever and amusing way to illustrate genetic dominance. One participant stated, "I think it's good to have it illustrated." Participants also indicated that the cartoons were appropriate for adult readers. One participant stated, "The cartoons were serious enough."

Although there was a generally favorable response to the inclusion of the cartoons, a second theme that emerged was a need for increased clarity. In some cases, respondents felt that a cartoon could be altered in order to be clearer. For example, when Fig 4 (mutated gene appearing to dominate a conversation with a normal gene) was presented, one participant responded, "The normal gene looks too cross to be dominated. He doesn't look submissive at all." In other instances, participants expressed uncertainty about what the cartoon was supposed to represent as well as its relationship to the accompanying genetic concept, even after hearing the genetic counselor's explanation of the cartoon, because the cartoon was too simple. For example, when Fig 6 was presented, one participant asked, "Does that mean that genes are on top of the chromosome or within?" Participants expressed a preference for simple illustrations that still conveyed the complexity of genetics, as with Fig 8, about which one participant stated, "It's very detailed but simple. It does a good job of explaining it." This desire to get a sense of genetic complexity was also demonstrated when Fig 1 (a photographic reproduction of chromosomal pairs) was presented with Fig 2 (a cartoon of a pair anthropomorphized chromosomes). One participant responded that Fig 1 "looks like it has parts to it but [the second]

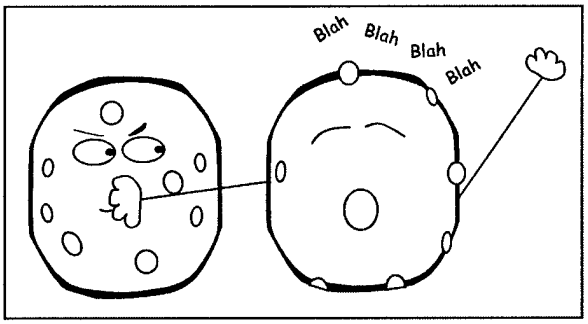

Fig 4. — A new image created for the revised information packet to demonstrate the concept of genetic dominance.

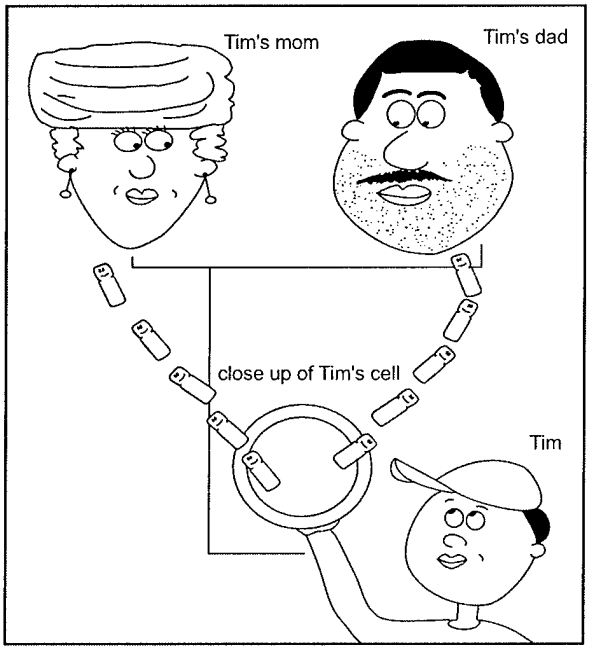

Fig 3. — A new image created for the revised information packet that described how chromosomes are inherited from parent to child.

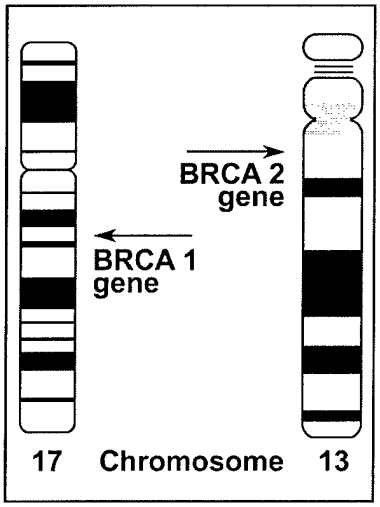

Fig 5. — An image from the original information packet showing the location of the *BRCA1/2* genes on the chromosomes.

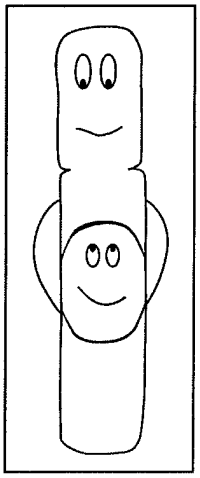

Fig 6. — A new image of a gene living on a chromosome. This image was intended to replace Fig 5.

doesn't. I'm fascinated with the first one." Another participant stated that Fig 1 "shows more of a whole picture to me." Another participant felt that Fig 2 "would insult" her intelligence.

Study 1 Discussion

Rapid focus group methodology enabled the authors to obtain specific information regarding the utility and appropriateness of images for the revised information packet. For the information packet revision, it was particularly important for the authors to know whether the cartoons were appropriate for its intended audience of adult breast cancer patients and inoffensive in light of some humorous elements. There was consensus among focus group participants that cartoons were appropriate but also that the cartoons could be made clearer. The rapid focus allowed the authors to reach a particular objective, ie, obtaining feedback that could be immediately incorporated into revision efforts. As a result of the focus group, several changes were made, including the deletion of Figs 2 and 6. Fig 4 was changed according the group's responses.

Several limitations of this study must be acknowledged. First, field notes rather than audiotape recordings were used to record participant responses. Reliance on notes may have introduced a bias in the responses recorded and, subsequently, in the interpretation of these responses. Second, a small number of breast cancer survivors were included in the focus group, and it is unclear how representative they were of the information packet's target audience of African American survivors, especially those with low reading skills. Moreover, the educational level of the participants was high, and their level of genetic knowledge before the focus group is unknown. However, these factors may be balanced by the fact that participants did not provide feedback to text but to images, so education and reading level may be less relevant in this case.

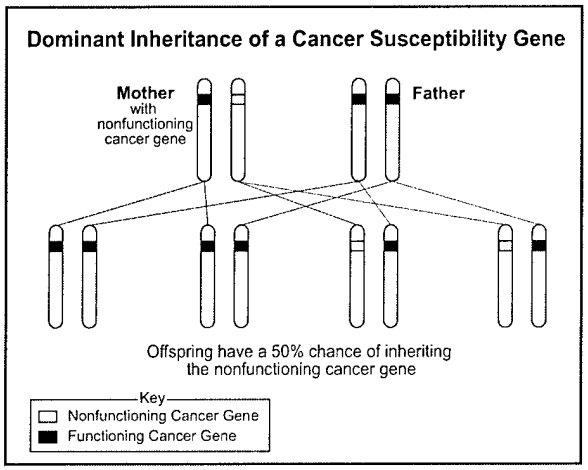

Fig 7. — An image from the original packet demonstrating dominant inheritance of a cancer susceptibility gene.

Study 2

Methods

In Study 2, a revised revised information packet that incorporated the feedback of the focus group in Study 1 was reviewed by African American adults with low literacy skills.

Participants

Participants were adult students in a literacy program sponsored by a local library system based in the Harlem area of New York, NY. The goal of this program is to serve adults who are nonreaders or beginning readers and writers by providing instruction in small groups, facilitated by volunteer tutors who are recruited, trained, and supported by professional staff members. Review of the revised information packet was consistent with the literacy program's goal of general health education.

The revised information packet was reviewed by 5 African American participants (3 men and 2 women) with an age range of 27 to 55 years. All participants were students in the literacy program and attended sessions at the library twice a week.

Materials and Measures

Participants reviewed the first 6 pages of the information packet. These pages contained sections discussing the major risk factors for breast and ovarian cancer and an introduction to genetics and included 1 graph and 3 cartoons (Figs 3, 4, and 8). This one section was selected for review due, in part, to time constraints within the class. It

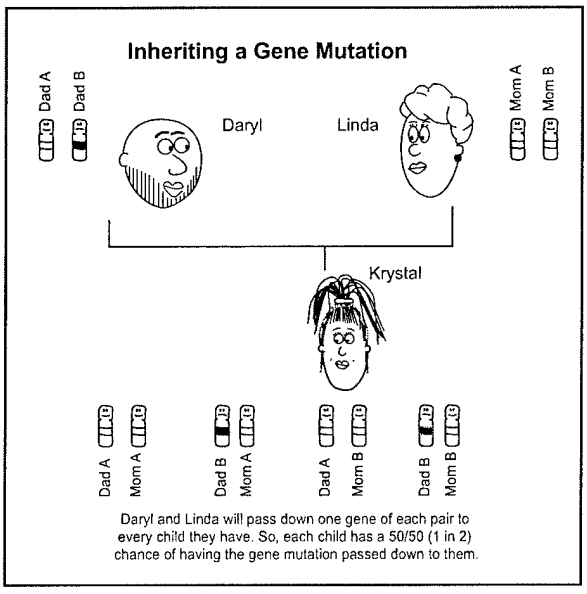

Fig 8. — Also demonstrating dominant inheritance of a cancer susceptibility gene, to replace Fig 7.

was also selected because, as the introduction to genetics, it contained more genetics-related terms and concepts compared with the rest of the information packet. Participants were asked to complete a 6-item evaluation of the information packet based on items in an assessment tool developed by Guidry and colleagues.[17] Although this tool is intended for professional-level reviewers of cancer education materials, in the current study we administered these items to the adult learners whose responses may be the best indicators of the information packet's readability.

Procedures

Copies of the revised information packet were submitted to the literacy program. Each copy began with instructions informing participants of the purpose of the booklet and that they were being asked to read a section of the information packet to make sure that it "is easy to understand and the language is down-to-earth." Through an agreement with the leadership of the literacy program, participants were asked to review the information packet during class time under the guidance of program tutors. Participants were also encouraged to provide general comments about the information packet content.

Results

Four of the 5 participants agreed that the information was presented in a way that was easy to understand and follow, that the font was easy to read, and that images in the information packet were appealing. Additionally, all participants agreed that the print size was easy to read. However, when asked how well they understood the meaning of all the words used in the booklet, all participants reported "a little" or "not at all." Also, when asked how much they liked the way the materials looked, 4 of the 5 participants reported "a little" or "not at all."

Study 2 Discussion

The ratings provided by adult learners provided vital information regarding the effectiveness of applied strategies to increase the readability of the information packet. Although these participants agreed that elements of the format and presentation facilitated comprehension, they largely reported that many words were difficult to understand. It was unclear whether lack of understanding was due to the use of words specific to genetics but clearly defined, or whether there were other, more common words that could have been substituted. In any case, this feedback suggested to the authors that the use of genetic jargon might be reduced and further revision was required. It is important to note that while the adult learners were given the information packet with only a brief explanation of its purpose, the information packet's actual target audience will receive the information packet after participating in a 2-hour genetic counseling session that will have already introduced all of the medical and genetics-related terms presented in the packet. It is possible that the exposure to these terms in the session will facilitate comprehension when the packet is later read.

Participants also generally did not like the way the materials looked. This may have been due to the fact that the information packet was not in color and did not look like a typical health-related brochure. This remains unclear as more specific feedback was not provided on these aspects. The failure to obtain more detailed feedback from participants is one limitation of this study. A second criticism that may be made of the study is that participants were asked to review only part of the information packet. Had the participants reviewed the entire packet, reports of comprehension may have been different. However, it may be argued that since comprehension of the first 6 pages was low, it is unlikely that comprehension of the rest of the packet would have been greater. A final limitation that may be noted is that there is no information on whether participants' knowledge of breast cancer genetics increased based on review of the information packet section. A pre- and post-test of such knowledge would have provided valuable information about reading comprehension.

Although feedback was somewhat limited, it provided an indication of how others with low reading ability might respond to the revised information packet and warranted continued efforts to improve readability as well as the appearance of the information packet. Based on participants' ratings, the text underwent a second revision. The final information packet was 25 pages long and included 8 pictures and 1 graph. A glossary and listing of patient resources was also included. Even after applying diverse strategies to increase readability, the final packet had a Flesch Reading Ease score of 64.8 and a Flesch-Kincaid Grade Level of 7.7. In exploratory analyses, the deletion of genetic terms and advanced medical terms improved readability somewhat (Flesch Reading Ease score = 70.7, Flesch-Kincaid Grade Level = 6.7).

General Discussion

The two studies reported here are among the first to describe efforts to reduce the readability gap between the advanced language often used in cancer genetics materials and the low literacy levels of a considerable portion of the US population. In the first study, a focus group of breast cancer survivors suggested that while the cartoons created for the packet were appropriate, some needed to be clearer in terms the concepts they were intended to convey. The focus group was a source of detailed responses that enabled the authors to make decisions regarding which images to retain, eliminate, or modify. In the second study, the ratings of adult learners suggested difficulty

with word comprehension in spite of the inclusion of definitions and a glossary. As a result of the evaluation-guided efforts described here, the readability of the final information packet improved significantly. Although the packet was not at a 5th-grade reading level, the 7th-grade reading level achieved is considerably lower than the college reading level required by the original information packet and the reported reading levels of informed consent documents for *BRCA1/2* testing.[12]

Although these studies provided valuable information that guided the revision of the information packet, it is important to reiterate the general limitations of both studies. First, only 3 participants were African American breast cancer survivors, the group that is the information packet's target audience. The inclusion of more constituents of this group might have provided a better indication of how actual TACT participants would evaluate and interpret the information packet. Second, although those who participated in the evaluation shared key characteristics with the packet's target audience, it is unclear how similar their responses were to potential responses from African American breast cancer survivors as a group since there is no published data on education or literacy levels of African American breast cancer survivors. Since limited sociodemographic data were collected from study participants, it is unknown how representative the participants were of the target audience. Also, the sample sizes of both studies were small, so even if the groups included in the evaluation were demographically very similar to the packet's target audience, generalizability is unclear. Finally, although we are collectively experienced in developing and testing cancer-related interventions, these studies are among our first efforts in developing printed materials that are appropriate for a wide range of reading levels. However, it is likely that many professionals developing cancer genetics materials have limited experience in addressing readability issues, and this fact should not preclude efforts among professionals to increase readability.

In spite of these limitations, there were several advantages to the evaluation approach reported here. First, it is common practice for interventionists and researchers to evaluate readability through quantitative methods and formulas rather than through the feedback of individuals.[14-17] Therefore, the approach used in the two current studies is a significant departure from methods used in previous readability evaluations. It is also consistent with a participatory research model that stresses substantive participation by those for whom materials are intended.[23] A second advantage of the studies presented here is the two-stage approach to evaluation in which the information packet's images, which were integral to comprehension, were evaluated first. Only after obtaining feedback on the images was the packet evaluated in its entirety. A third advantage was the use of methods and measures that enabled rapid data collection.

Future efforts to increase the readability of cancer genetics materials may address at least one unresolved issue in the current studies: the inclusion of genetics-related terms that inflate objective readability scores. It seems compulsory to include in such terms in educational materials as the goal of such materials are to increase patient knowledge. Additionally, many of these terms are commonly used by medical professionals. Thus, a patient's familiarity with these terms may assist in making interactions with medical professionals more informative and productive. However, it is possible that these terms may impede a patient's comprehension of materials because they are advanced terms that are more a part of professional jargon vs everyday language. Future studies may carefully assess the extent to which patients' understanding of cancer education materials are enhanced or undermined by the inclusion and exclusion of these terms.

More generally, future efforts to increase the readability of cancer genetics materials may make greater efforts to draw on the perspectives of the constituents who represent the materials' target audience. Such efforts are crucial as those who develop the materials and have expertise in the topic may underestimate the topic's complexity, thus limiting the ability to assume the perspective of a naive reader. Constituent evaluation, therefore, has the potential to identify areas in which further explanation and clarification is necessary. Finally, the studies reported here demonstrate the value of collaboration with formal organizational networks such as literacy programs and cancer patient/survivor groups. These networks may assist in the identification of individuals appropriate for inclusion, and they typically have communication mechanisms in place (eg, regular meetings, mailings) that facilitate actual data collection.

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ORIGINAL COMMUNICATION

EXPERIENCES OF RACIST EVENTS ARE ASSOCIATED WITH NEGATIVE HEALTH CONSEQUENCES FOR AFRICAN AMERICAN WOMEN

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This study investigated whether experiences of racist events were related to psychological distress, negative health behaviors, and health problems. Participants were 71 African American women (mean age 44.4) who were recruited from an urban cancer-screening clinic as part of a larger longitudinal study on familial risk of breast cancer. Participants completed three study assessments, approximately one month apart, and data were collected via self-report. Correlational analyses revealed that past year and lifetime racism were both related to psychological distress. Among smokers and drinkers, past year racism was positively correlated with number of cigarettes and drinks consumed. Lifetime racism was negatively related to perceived health, and positively related to lifetime history of physical disease and frequency of recent common colds. Analyses using a general linear model revealed that these relationships were largely unaccounted for by other variables. In addition, demographic variables such as income and education were not related to experiences of racism. The results suggest that racism can be detrimental to African American's well being and should be investigated in health disparities research. *(J Natl Med Assoc.* 2003;95:450-460.)

Key words: racism ♦ health disparities ♦ chronic stress

Numerous authors have commented on the ways in which longstanding racism in American society affects African Americans.[1-10] A wide-ranging literature reveals that African Americans face denigrating images of themselves and their culture in the dominant society, are subjected to discrimination on institutional levels, and experience acts of prejudice (which may include physical violence) on an individual level.[11-21] Moreover, the insidious nature of racism means that African Americans from varied backgrounds are affected.[22-24] As a result, racism has been conceptualized as a chronic stressor in the lives of African Americans.[25] The well documented health disparities between African Americans and European Americans in the United States[26-30] may be due, in part, to experiences with racism.

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If racism represents a chronic stressor, the literature on the effects of chronic stress would suggest that it could have an adverse effect on both the mental and physical health of African Americans.[31] As yet, however, little research has examined how experiences of racism may affect health outcomes. A few studies have provided evidence of a relationship between racism and mental health. For example, data from the National Survey of Black Americans showed that perceptions of racism and racial discrimination were associated with poorer mental health.[32] In addition, discrimination has been shown to be related to lower levels of perceived mastery and higher levels of psychological distress.[33, 34] Other studies report a relationship between experienced racism and intrusive thoughts about the racist event.[35] These studies are likely to have underestimated the extent of the problem, because they utilized single-item assessments of racism, and this approach tends to underestimate discrimination.[36]

For physical health, the literature on the effect of racism is more sparse.[37, 38] In population samples, one recent study found that among a group of varied ethnicities, perceived racism was related to poor self-perceived health status.[39] An association between discrimination and cardiovascular outcomes has been reported, although not in a dose-reponse relationship.[40,41] Some authors have offered theoretical models of how racism might lead to chronic illnesses such as prostate cancer,[42] but researchers have yet to investigate how these models bear out in practice.

Given that psychological stressors affect health behaviors, some investigations have studied how racism relates to health behaviors. Two studies[43,44] examined the association between racism and smoking. The data shows that African Americans who experience more racial discrimination smoke more. Another study[45] found that transit workers of varied ethnicity who reported higher discrimination also reported more drinks per month, heavy drinking, and alcohol dependence than those who reported less discrimination.

The present study sought to build upon the current evidence by examining the role of experienced racism in psychological adjustment and physical health. Our investigation is undergirded by the biopsychosocial model proposed by Clark et. Al,[25] wherein the perception of racism is hypothesized to lead to adverse health outcomes through psychobiological stress responses, or negative health behaviors. More specifically, we looked at psychological distress, negative health behaviors (drinking, smoking), and health problems (perceived health, frequency of lifetime illness, and frequency of common colds). We hypothesized that higher perceived levels of racist events would be positively related to drinking and smoking behavior. In addition, because chronic stress has been found to be negatively related to physical health and the common cold,[46-49] we hypothesized that racist events would also be positively related to perceived health, lifetime history of disease and the common cold.

METHODS

Study Design and Sample

The data were gathered as part of a larger longitudinal investigation of women with different levels of familial risk for breast cancer. However, because including family history of breast cancer as a covariate in preliminary analyses did not alter the significant effects reported below, it was not included in the final analyses.

Participants were recruited from an urban cancer screening clinic (The Breast Examination Center of Harlem) that provides comprehensive diagnostic screening services to members of the Harlem community. All services are provided at no out of pocket expense to the client. Ninety-seven percent of the clinic's clientele is Black or Latina, and at the time data was collected for this study, the staff was 95% Black or Latino(a).

The sample was comprised of 71 African American women with a mean age of 44.4 years (range = 26 -72). Eighty-five percent of the sample completed at least some high school, 63%

were currently employed, and 30% were currently married. Income (household) was as follows: < $10,000 (n=12); $10,000-$19,999 (n=31); $20,000-$39,999 (n=39); $40,000-$59,999 (n=17); $60,000-$100,000 (n=8); >$100,000 (n=1). For statistical analyses, these categories were collapsed into two (<$40,000, ≥ $40,000).

To be eligible, participants had to be 25 years or older, be able to read/write English and be able to provide meaningful informed consent. To reduce sources of heterogeneity in outcome variables, women currently taking prescription medication other than hormone replacement therapy or birth control pills were excluded. Women taking over-the-counter medications were not excluded.

Participants were recruited from the clinic on

Table 1. PERCENTAGE OF WOMEN WHO EXPERIENCED RACISM IN THE PAST YEAR AND IN THEIR LIFETIME

Type of racism	Lifetime	Past Year
Treated unfairly by neighbors	30	18
Made fun of, picked on, pushed, shoved, or hit	36	12
Forced to take drastic steps (filing lawsuit, moving away)	37	18
Treated unfairly by people that you thought were your friends	38	27
Accused or suspected of doing something wrong (stealing, cheating)	46	27
Treated unfairly by employers, bosses, supervisors	47	34
Gotten into an argument or fight about something racist	54	17
Called a racist name	55	15
Treated unfairly by co-workers, fellow students, colleagues	61	27
Treated unfairly by teachers and professors	62	22
People misunderstood your intentions and motives	63	47
Treated unfairly by people in helping jobs (doctors, case workers)	66	34
Wanted to tell someone off for being racist but didn't say anything	66	49
How different would your life be now if you HAD NOT been treated u	68	49
Treated unfairly by institutions (schools, police, courts)	70	39
Been really angry about something racist	81	50
Treated unfairly by people in service jobs (store clerks, waiters)	83	69
Treated unfairly by strangers	84	67

Note: Percentages reflect proportion of women who endorsed item (at any degree), as opposed to endorsing "Never" or "Not at all". Item content is abbreviated for space.

scheduled clinic days by an African American female researcher (JG), as follows. The study was briefly described to a group of women in the waiting room. Interested women approached the researcher who verified eligibility criteria and obtained informed consent. Less than 10% of interested women declined participation and consistent with our IRB regulations we have no information on these women. After agreeing to participate, all were given an appointment to meet with the researcher three to four weeks afterwards, to complete study questionnaires at a time when no clinical services were provided. None of the participants had been found to have breast abnormalities. Because volunteers were accepted into the study, and women were not individually invited to participate, refusal rates are not available.

After the first scheduled visit, participants returned twice more to the clinic, solely to complete study assessments, and visits were approximately one month apart. We conducted multiple assessments of critical outcome variables to increase reliability over "one shot" assessments that are more common in the literature. In addition, by aggregating across three assessments, we increased the base rate of outcome variables (e.g., colds). Measures were completed while an investigator was present, so that questions could be answered. However, participants had the option of completing the demographic questionnaire at home and returning it later. Participants were offered $20 plus the cost of public transportation to and from each visit.

Because so few (n=3) of the women who began the study (n=74) did not complete all assessments, it was not appropriate to analyze differences between "completers" and "non-completers" on outcome variables.

Study Variables

All questionnaires were written self-report measures. A standard demographic questionnaire (50) was used to obtain information such as age, marital status, education, employment, and income.

General psychological distress in the past three weeks was assessed with the Brief Symptom Inventory (BSI), a 53-item standardized measure with strong internal consistency.[51] A general distress index was calculated by obtaining the mean of all items, with higher numbers indicating greater distress. These scores were averaged across three assessments.

Lifetime smoking status was assessed with a single item from the National Health Interview Survey:[52] "During your lifetime, have you smoked at least 100 cigarettes (5 packs)?" To provide an indication of recent smoking, at each study assessment, participants reported how many cigarettes they smoked: "today," "yesterday," "two days ago," and "three days ago". Occurrence of alcohol consumption was reported for the past month (yes/no), and recent quantity consumed was assessed, as was recent smoking. The responses to these questions were averaged across the three visits.

The women's perception of their own health was assessed at the initial visit, with a well-established single item assessment: "In general, how is your health compared to other people your age?"[53, 54] Responses were given with a 5-point Likert scale with "1" representing "Excellent" and "5" representing "Poor". To assess lifetime history of disease, participants reported the occurrence of ever having been diagnosed by a doctor with a system by system checklist of diseases (e.g., gastrointestinal, immunological, infectious, endocrine). The total sum of these lifetime illnesses was used as another index of physical health. During each study assessment participants reported the occurrence and frequency of colds in the past three weeks. These responses were averaged over the three assessments, thus covering a nine week interval. Self-reported cold numbers have been found to be valid in a previous study that confirmed such reports with physical exams.[55]

Experiences with racism were assessed with the Schedule of Racist Events (SRE) [34, 43] at the

first study assessment. The scale is an 18-item self-report inventory that measures the frequency with which African Americans have experienced racist events (on a 6-point scale ranging from "Never" to "Almost all of the time"). Item content is listed in Table 1. For each item, ratings for

Table 2. BIVARIATE CORRELATIONS BETWEEN EXPERIENCED RACISM AND HEALTH OUTCOMES

Outcome Variable	Past Year Racism		Lifetime Racism		Appraisal of Stress	
	Bivariate correlation	p value	Bivariate correlation	p value	Bivariate correlation	p value
Psychological Distress	.31	<.01	.40	<.001	.32	<.01
r^2	**.09**		**.16**		**.10**	
Quantity of cigarettes	.37	<.05	.13	.46	-.005	.97
r^2	**.14**		N/A		N/A	
Quantity of alcoholic beverages	.40	<.05	.23	.20	.11	.55
r^2	**.16**		N/A		N/A	
Perceived health	.19	.12	.27	<.05	.01	.95
r^2	N/A		**.07**		N/A	
Lifetime history of disease	.03	.79	.23	<.05	.03	.79
r^2	N/A		**.05**		N/A	
Common cold frequency	.38	<.01	.41	<.01	.25	.08
r^2	**.14**		**.17**		N/A	

Note: Relations to quantity of cigarettes and alcoholic beverages, and frequency of colds is reported for those individuals who smoked, drank, or had a cold during the study. Means were as follows: quantity of cigarettes= 63.0; alcoholic beverages=2.67; colds=1.66.

r^2 was calculated only for significant correlations. N/A, not applicable because correlations were not significant.

the past year and lifetime are requested, as well as the degree of stress associated with each experience. The mean score for responses in each of the three facets are computed.

Statistical Analyses

To investigate group differences (e.g., past year racism in smokers vs. non-smokers), analysis of variance (SAS statistical package) was used. To investigate the strength of the association between racism and health outcomes, Pearson-product moment correlations were computed. To determine whether discovered relationships could be explained by other variables, SAS general linear model (GLM) was used as a regression model. Thus, if a significant relationship was discerned between experienced racism and a health outcome, the GLM was used to determine if this relationship persisted after controlling for other relevant variables.

RESULTS

Descriptives

The mean for past year racism (PYR) was 1.71 (SD= .65), lifetime racism (LTR) was 2.36 (SD= .98) and appraisal of stress (AOS) was 2.79 (SD=1.32). Given that a score of "1" indicates "Never" experiencing the racist event listed in the item, and "2" indicates "Once in a while," there was not a high level of racism experienced in the sample. Bivariate correlational analyses revealed no significant relationships between any demographic variables (i.e., age, marital status, education, income, or employment status) and any facet of experienced racism. Income was positively related to lifetime history of disease, $r = .23$, $p < .01$, and cold frequency, $r = -.25$, $p < .05$. Income was not significantly related to drinking or smoking.

Table 1 shows the item-by-item frequency of past year and lifetime experienced racism in the sample. As can be seen, most participants had experienced some racism in their lives, including more severe events such as having to take drastic steps regarding the racist event (e.g., lawsuit).

Health Outcomes and Racism

Table 2 shows the bivariate correlations, significance levels and r^2 values for the three facets of experienced racism and each health outcome. As can be seen, experienced racism was positively correlated with overall psychological distress.

None of the facets of experienced racism were related to ever being a lifetime smoker. However, for individuals who were smokers (n=34), PYR was related to how many cigarettes were smoked. Distress did not account for the relationship between PYR and smoking, as adding it to the model did not eliminate the significance of the relationship, $F^{2, 31} = 5.03$, $p < .05$, as shown in Table 3.

PYR was related to whether or not women drank in the past month, but this was an inverse relationship; non-drinkers experienced more racism than drinkers, $F^{1,69} = 5.44$, $p < .05$. Again, however, among drinkers (n=33), PYR was positively related to how many drinks were consumed, as shown in Table 2. The relationship between PYR and quantity of drinks did not appear to be accounted for by distress; adding distress to the model did not eliminate the significance of the relationship, $F^{2, 30} = 5.78$, $p < .05$, as shown in Table 3.

With regard to perceived health, women who had experienced more LTR rated their overall health as poorer, as shown in Table 2. When distress, drinking and smoking were added to the model, the relationship between LTR and perceived health was no longer significant. Drinking and smoking did not account for the relationship, as racism remained significant with these variables. However, distress appeared to be a mediator, as including it by itself in the model eliminated the significance of the relationship, $F^{2, 67} = 2.12$, $p = .15$, as shown in Table 3.

LTR was positively related to lifetime history of disease, as shown in Table 2. Including distress, smoking and drinking in the model did not affect this relationship, $F^{4,65} = 4.88$, $p < .05$. For the common cold, only PYR was positively relat-

ed to having a cold in the nine weeks assessed, $F_{1,68} = 5.33$, $p<.05$. However, among women who had colds (n=47), both PYR and LTR were significantly related to the *number* of colds women experienced (see Table 2). The relationship between racism and cold frequency was not explained by distress, drinking or smoking. After adding these variables to the model, PYR still remained significant, $F_{4,42} = 4.83$, $p <.05$, as did LTR, $F_{4,42} = 5.09$, $p<.05$, as shown in Table 3.

Discussion

The results of the present study supported the hypotheses that individuals who reported having experienced racism would have higher levels of psychological distress, negative health behaviors and physical health problems. More specifically, greater experienced racism (higher scores on the Schedule of Racist Events) was associated with higher distress, greater alcohol and cigarette consumption, more common colds, and more lifetime illnesses. The study's findings are concordant with those in the literature, but also introduce new findings with drinking behavior, and, to the best of our knowledge, provide the first data to show a relationship between experienced racism and physical health outcomes outside of the cardiovascular system.

It is important to note that experienced racism did not vary significantly by a variety of demographic variables including age, income or education, evidence of the widespread nature of racism. It is also noteworthy that the women in this sample did not report extreme levels of experienced racism. Some researchers contend that recognition of discrimination may adversely affect self-esteem and perceptions of control, and as a result, these experiences may be denied or minimized.[37] The vast majority of the present participants reported having experienced some form of racism during their lives, including having to take drastic steps such as lawsuits to remedy the situation. It is possible that these reports even underestimate the actual level of experienced racism. Given that the relationships were found with relatively low levels of racism, African Americans who experience more severe levels may be at even greater risk for poor health outcomes.

Experiences with racist events accounted for a fair amount of variance in health outcomes (r^2 values). It is not surprising that only 5% of the variance in lifetime history of disease was attributable to lifetime racism, given the important role of other factors such as lifestyle (e.g., diet, exercise) genetics, immune function, physical environment, etc. However, that even 5% of the variance is accounted for by lifetime experienced racism highlights the effect racism has on African Americans. Psychological distress, quantity of cigarettes and alcohol consumed, and frequency of common colds showed higher r^2 values. Again, a range of 14%-17% is not trivial when we consider the number of other variables that may be related to these outcomes. In addition, that racism experienced over a *lifetime* accounted for 16% of the variance in distress experienced in the past *two weeks* is notable.

Racism and Health Behaviors

In this study, experienced racism was not related to whether or not women smoked. However, it did predict whether women were drinkers, with those who experienced *less* racism being more likely to drink. This was an unexpected finding. Based on their empirical data, Jackson et al.[32] argue that individuals who perceive whites as wanting to keep blacks down may be more vigilant when it comes to their own physical health; they are more likely to recognize the importance of looking out for themselves. This is a possible explanation for the inverse relationship found in this study. Many African Americans are aware of the disparities in alcohol sales among African American and European American neighborhoods, [56] as well as the targeted marketing of malt liquors and other alcoholic beverages.[57] Thus, those who have more individual experience with racist events might be more vigilant in avoiding substances that are readily connected to racism.

The more consistent finding was that women who engaged in either drinking or smoking did so with increased frequency as a function of experienced racism. Interestingly, this relationship was not mediated by distress levels assessed here. It is possible that distress would act as a mediator if measured by an instrument other than the Brief Symptom Inventory. For example, race-related stress[58] may be more predictive for African Americans than general, global distress.

Racism and Physical Health

Experienced racism was related to lifetime history of disease and recent experience of common colds. The mechanisms behind this relationship between racism and physical illness bear further exploration. In this study, neither the higher lifetime history of disease, nor the higher frequency of common colds associated with experienced racism were mediated by drinking, smoking or general distress. It may be that experiences of racism lead to compromised immune functioning. Given that racism represents a source of substantial stress, exposures to racist events may have deleterious effects through multiple pathways.[25] Thus, the role of experienced racism as a contributor to health disparities should be investigated. Institutional racism results in inequalities in living conditions and access to health care,[59] which in turn results in poorer health status for African Americans. However, the present data suggest that individual experiences of racism may be a factor in the disproportionate burden of illness in the African American community. Moreover, conscious awareness of racism as a stressor may not be necessary to result in physiological stress responses. In our study, appraisal of stress due to racism was not related to health outcomes; rather, the frequency of racist events alone predicted negative health outcomes.

Table 3. RESULTS OF MULTIVARIATE ANALYSIS BETWEEN RACISM AND HEALTH OUTCOMES

Outcome Variable	Source	DF	Type III SS	Mean Square	F value	Pr > F
Quantity of cigarettes	Distress	1	195.67	195.67	0.07	.79
	PYR	**1**	**14319.01**	**14319.01**	**5.03**	**.03**
Quantity of alcoholic beverages	Distress	1	.652	.652	0.05	.82
	PYR	**1**	**71.45**	**71.45**	**5.78**	**.02**
Perceived health	Distress	1	2.32	2.32	3.07	.08
	Quant. alcoh.	1	.803	.803	1.06	.31
	Quant. cig.	1	2.47	2.47	3.26	.08
	LTR	1	1.38	1.38	1.83	.18
Cold frequency	Distress	1	.800	.800	1.15	.29
	Quant alcoh.	1	.174	.174	0.25	.62
	Quant cig.	1	1.16	1.16	1.67	.20
	PYR	**1**	**2.87**	**2.87**	**4.13**	**.05**

Limitations of the Present Study and Directions for Future Research

First, because this study is cross-sectional in design, causality between experienced racism and health outcomes cannot be established. Second, we used only self-reports for study variables (e.g., instead of endocrine measures of stress). However, as previously noted, self-reports of colds have been found to be reliable.[55] Third, the sample size was relatively small, and was comprised of urban African American women recruited from a cancer screening clinic, which limits generalizability. Finally, although we found no support for the possibility that relationships between experienced racism and health outcomes were due to confounding demographic variables, we cannot rule out the possibility that other demographic indices (e.g., insurance status, generational wealth) would have yielded different results.

African American men, as well as the larger community of individuals of African descent should be the subject of future research. Much of the research on racism has been conducted with African Americans, as opposed to individuals from the Caribbean or the African continent who reside in the United States. Clearly, it is unlikely that other groups in the Diaspora are immune to the effects of racism, and there may be a different picture regarding health consequences. For example, in the Caribbean, race is not often viewed as a deterrent to political or economic empowerment, and racism may not be experienced as much of a reality.[60] Thus, individuals from the Caribbean may not recognize racist behaviors as readily as African-Americans, as they may not have been sensitized to such events in the same way. If this is true, perhaps the same health outcomes would not emerge.

Future research should examine the effects of the more pervasive, "invisible" level of racism. Our study focused on immediate, individual-level racism: discrete experiences such as being called a racist name, or being discriminated against by service workers. Discrimination is not simply random acts of unfair treatment, but a socially structured and sanctioned phenomenon, justified by ideology.[61] This deeper level of racism, which structures the everyday life of American society, has direct bearing on quality of life issues such as nutrition, clothing, shelter, medical care, safety and education and is a source of substantial stress.[62] In addition, "vicariously-experienced" racism such as police brutality in the community is also likely to affect the emotional and physical health of African Americans. Indeed, some researchers have argued that the belief that one is living in a discriminatory society may itself be detrimental to health.[39]

Future research should also consider the variables that may act as mediators or moderators of the relationship between racism and health. As previously discussed, with the exception of perceived health, the relationships found in the present study were largely unaccounted for by other variables (e.g., general distress, smoking). While income was related to lifetime history of disease and cold frequency, this variable could not mediate the relationship between racism and these outcomes, as it was not significantly related to the predictor variable, racism. A mediating variable must be significantly related to both the predictor and outcome variables.[63] It is possible that variables that were not assessed in this study, such as physiological reactivity to acute stressors,[5, 64] or positive health behaviors, such as exercise or diet may play a role. Other variables that are likely candidates might be cultural identity and internalized racism. Internalized racism has been defined as the acceptance of negative messages about ability and intrinsic worth: ". . . it is characterized by their not believing in others who look like them, and not believing in themselves. It involves accepting limitations to one's own full humanity..."[65] African Americans who think poorly about themselves may be more likely to engage in negative health behaviors, having less belief in their intrinsic worth. It has been suggested that engaging in positive health behaviors is impeded not only by cultural oppression,

but also by internalization of those ideologies.[66]. Indeed, there is some evidence that internalized racism leads to negative health outcomes.[67]

Some data suggests that a non-Africentric orientation can be detrimental [68, 69] and other studies show that an Africentric orientation can be protective against negative health outcomes [70] and is positively related to health-promoting behaviors.[71] An individual's racial identity [72] or cultural worldview may be a moderating variable between experienced racism and health outcomes and should be examined in future studies. For example, perhaps individuals who are more inclined to expect racism develop a cognitive schema to deal with the stressor, whereas those who are surprised by incidents of racism suffer negative health outcomes. As research begins to determine the mechanisms involved in negative health outcomes, interventions can begin to be formulated. Ultimately, our goal may not be to eradicate racism, but to neutralize its negative effects on health.

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We are required to indicate that the views, opinions and findings contained in this report are those of the author and should not be construed as an official Department of Defense position, policy or decision unless so designated by other documentation.

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Posttraumatic Headache: An Exploratory Treatment Study

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Fourteen patients with posttraumatic headache (PTHA) were treated with a comprehensive treatment package targeting headache symptoms along with associated posttraumatic stress symptoms. Treatment consisted of some or all of the following depending on headache features: thermal biofeedback, electromyography biofeedback targeting the forehead and/or neck muscles, progressive muscle relaxation, education and cognitive–behavioral therapy. Mean improvement for the treatment group was 21%, whereas mean improvement for the wait-list group was −14% indicating a worsening of headache; however, the difference between groups was not statistically significant. There was a significant between groups difference on headache-free days. Within group results were modest with 29% mean improvement by the end of treatment. The reduction in headache index was significant. Minor reductions in psychopathology, most notably anxiety, were found after treatment. This study confirmed the treatment difficulties seen in this understudied population of headache sufferers, but offered hope for symptom relief.

KEY WORDS: posttraumatic headache; biofeedback; relaxation; cognitive therapy; posttraumatic.

Reports of incidence of posttraumatic headache (PTHA) following mild head injury range from 30 to 90%, with one third of all cases developing into chronic headache (HA; Ramadan & Keidel, 2000). The literature suggests that PTHA is similar to non-PTHA in both pathogenesis and presentation, therefore standard treatments are typically used yet, PTHA is one of the most difficult headache types to treat (Packard & Ham, 1994) and it is often excluded from psychological treatment studies.

Many of the studies conducted on this population are case studies or retrospective in nature. The majority of available information on the nondrug treatment of PTHA has examined some form of biofeedback. Many clinical observations support the use of biofeedback alone or in conjunction with medication, relaxation, and psychotherapy (e.g., Bennett, 1988;

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Packard & Ham, 1994). These clinical observations are in line with treatment studies of regular HA.

Success of biofeedback varies from study to study. Tsushima and Hawk (1978) used EMG biofeedback to treat seven patients with PTHA and found mild to moderate improvement in five of the seven. However, studies indicate that EMG and thermal biofeedback are less effective in chronic cases and in cases with fewer treatment sessions (Ham & Packard, 1996).

In general comparisons to non-PTHA sufferers, PTHA sufferers have less success in treatment. Compared to a group with non-PTHA tension-type headache, EMG biofeedback was less effective in the PTHA population (Tsushima & Hawk, 1978). A later study by Onorato and Tsushmia (1983) found similar results indicating that tension HA patients had better treatment outcome than the PTHA patients. Because this group is harder to treat than the regular HA population Tsushima and Hawk (1978) suggested that more treatment sessions might be indicated.

Successful results have been found in studies employing multiple treatment components (e.g., Duckro, Tait, Margolis, & Silvermintz, 1985; Hickling, Blanchard, Schwarz, & Silverman, 1992; McGrady, Bernal, Fine, & Woerner, 1983; Medina, 1992). An early study by McGrady et al. (1983) treated PTHA patients with medication, EMG biofeedback, and stress reduction therapy. Factors found to influence treatment response include high pretreatment tension levels, mild to moderate pain, faithful home practice, and psychological openness. Significant decreases in pain levels were seen in McGrady et al.'s sample.

Medina (1992) employed a comprehensive treatment package including medication, education, biofeedback, stress management, and physical therapy in a PTHA population whose pain was preventing them from working. Patients were seen one to three times a week for 1–3 months of individual therapy. Seventeen out of 20 of these patients successfully returned to work.

Hickling et al. (1992) used cognitive–behavioral therapy (CBT), support, relaxation, and biofeedback. If patients exhibited symptoms of PTSD, this problem was addressed. The number of sessions varied from 8 to 50, with a mean of 20. Findings indicated those with PTSD needed significantly more sessions (24.6, $SD = 15.4$ vs. 10.8, $SD = 2.2$). Eight of the 12 patients improved significantly.

A case study by Duckro et al. (1985) employed several techniques including CBT and EMG biofeedback, along with education. Some goals of the treatment were to reduce emotional stress, offer an alternative explanatory schema and explain the role of medication. In this particular case, the multicomponent treatment was effective.

It has often been important to target other problem areas in addition to the headache. The case study by Duckro et al. (1985), along with many of the other multicomponent studies previously examined have used some type of coping/stress management. Martelli, Grayson, and Zasler (1999) suggest stress is a component that clinicians have the most power to target. Factors that could influence treatment outcome include personality (e.g., manipulative–avoidant pain behavior; Onorato & Tsushima, 1983) or untreated comorbid disorders such as PTSD or depression (Hickling et al., 1992).

Based on the limited number of controlled treatment studies, it appears that psychological treatment can have some benefit in this population, though treatment effects may not be as great as in HA populations other than PTHA. Available studies indicate that this population may need a greater number of treatment sessions, along with targeting comorbid symptoms of PTSD and/or depression if applicable.

The purpose of the present study was to implement a treatment program that was comprehensive enough to bring relief to this refractory headache population. Based on the literature, it was thought important to include an adequate number of sessions, along with focusing treatment on comorbid symptoms such as PTSD and depression. Treatment also focused on stress management aimed at reducing headache, along with reduction of other psychological symptoms such as PTSD, depression, and anxiety. A study of this type fills a gap in the literature, as there is a lack of controlled, prospective treatment studies in this population. Of the available treatment studies reviewed that examined or included PTHA, only one (Tsushima & Hawk, 1978), appears to be both controlled and prospective in nature.

METHODS

Participants

Participants were recruited through several channels including a Federally funded motor vehicle accident (MVA) survivor treatment study, a Federally funded headache assessment study, physician referrals, and newspaper ads. In addition to meeting Headache Classification Committee of the International Headache Society [IHS] (1988) criteria for PTHA, all participants met the following criteria: occurrence of HA for at least 6 months, age 18 or older and been seen by a physician for their headache. Additionally, participants were given a diagnosis of migraine, tension, or mixed headache type based on their headache features. The following exclusionary criteria applied: past or current psychotic symptoms, past or current manic symptoms, and current alcohol or substance abuse/dependence.

A total of 19 participants were seen for an initial assessment. Fourteen of these participants completed the assessment and started treatment. The final sample was composed of 12 females and 2 males, of average age 43 years (range 23–74). The sample was 79% Caucasian. Of the 14 treated participants, 12 experienced HA as the result of an MVA. Nine met IHS criteria for PTHA without confirmatory signs, whereas five met IHS criteria for PTHA with confirmatory signs. HA features were examined to establish secondary diagnoses. Nine of the participants met IHS criteria for tension-type HA, four for mixed HA, and one for migraine. All HA diagnoses were independently confirmed by a board certified neurologist (DJS). Additionally, the neurologist reviewed medication diaries in order to rule out analgesic rebound headache (see Table I for participant characteristics).

Measures

Headache frequency and intensity ratings were gathered on pencil and paper diaries. This HA rating scale was developed by Budzynski, Stoyva, Adler, and Mullaney (1973) and validated by Blanchard, Andrasik, Neff, Jurish, and O'Keefe (1981). Headaches were rated on a 6-point scale (0 = *no HA* to 5 = *intense incapacitating HA*) four times daily. Ratings from the diary were converted to a composite score (the headache index score) which takes into account both frequency and intensity. Headache index score served as the primary treatment outcome measure. Analysis also included an examination of headachefree days before and after treatment.

Participants recorded medication consumption pre-, post-, and during treatment. Medications were scored based on the system developed by Coyne, Sargent, Segerson, and

Table I. Participant Characteristics and Individual Pre, Post, and 2-Month Follow-Up Headache Index Scores

ID no.	Age	Sex	HA type[a]	Months with HA	Pre-HA index	Post-Wait-list HA index	Post-Phase I HA index	Post-Phase II HA index	Follow-up HA index[b]	% Improvement post[c]	% Improvement follow-up[c]
1	44	F	1a	64	16.8	18.1	11.8	—	—	30	—
2	50	F	1a	44	11.2	10.1	9.1	10.1	9.3	10	17
3	23	M	2a	55	5.3	3.6	4.6	3.4	3.9	35	26
4	43	F	2c	62	8.1	6.6	1.8	—	0.9	78	89
5	33	F	2c	84	6.9	8.0	7.2	5.3	4.4	24	37
6	33	F	2a	7	5.8	5.8	4.4	—	—	25	—
7	65	F	1a	88	6.9	—	4.1	—	6.9	40	0
8	41	F	1b	51	6.7	—	2.9	—	2.6	57	61
9	74	M	1a	12	9.9	—	13.9	14.9	11.7	−51	−19
10	28	F	2a	14	5.5	—	3.3	—	4.4	40	21
11	29	F	2a	63	2.1	5.1	1.1	—	1.9	47	10
12	45	F	2c	13	1.3		2.5	—	1.1	−94	11
13	36	F	2a	121	1.9		0.0	0.3	0.1	85	92
14	56	F	2c	25	2.6		1.3	—	1.4	50	45
Means	43			50	6.5	8.2	4.9	6.8	4.2	27	32

[a] 1 = Chronic PTHA with significant head trauma and/or confirmatory signs; 2 = chronic PTHA with minor head trauma and no confirmatory signs; a = tension HA; b = migraine; c= mixed HA.

[b] Two participants failed to return 2-month follow-up data.

[c] Improvement based on pretreatment scores; posttreatment was the last session (Phase I or II) for each participant—number of sessions ranged from 8 to 18.

Obourn (1976). An average medication consumption score was obtained from pre- and posttreatment periods. Participants were asked to refrain from starting new medication during the study, in order to avoid confounding the results.

Participants completed various reliable and valid paper and pencil measures designed to tap into the following domains including depression, anxiety, PTSD, and physical symptoms. Administration of all measures occurred at the following points: pretreatment, posttreatment (Phases I and II), and 2-month follow-up.

Measures of depression and anxiety were obtained from the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) and the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970), respectively. Posttraumatic stress symptoms were measured with the PTSD Checklist (PCL-S; Weathers, Litz, Herman, Huska, & Keane, 1994).

The Postconcussion Syndrome Checklist (PCSC), allowed for examination of physical symptoms common after head injury such as dizziness, fatigue, visual disturbance, etc. (Gouvier, Cubic, Jones, Brantley, & Cutlip, 1992). This measure allows for examination of frequency, intensity, and duration of symptoms. Total scores were used in this analysis. This instrument is reliable and valid (Gouvier et al., 1992).

Treatment

There were two phases to this treatment. The first phase was the headache treatment portion of the study. Treatment consisted of TBF and progressive muscle relaxation (PMR) for those with migraine features or tension and migraine features (i.e., mixed headache), and EMG biofeedback and PMR for those with tension headache. Based on previous research suggesting the usefulness of EMG biofeedback for neck pain (Blau & MacGregor, 1994) any participants with neck pain regardless of headache type received EMG biofeedback targeting the neck area. The TBF, EMG, and PMR components of treatment were conducted in a fashion similar to that described by Blanchard and Andrasik (1985). Also, all participants received an education component and a cognitive therapy component. The cognitive therapy component (also described in Blanchard & Andrasik, 1985) is based on Beck, Rush, Shaw, and Emery's model (Beck, Rush, Shaw, & Emery, 1979) and has been found to be useful for treating depression, emotionality, and irritability (all of which are significant in the PTHA population).

This headache treatment phase of the study lasted for 6 weeks (two times a week for 12 total sessions). The first four sessions consisted of PMR. Cue-controlled relaxation was introduced in the sixth session. Biofeedback (TBF and/or EMG) was introduced in the fifth session followed by one or two sessions of cognitive therapy only. The last three or four sessions contained all treatment components. Treatment was administered by the first author (KT), an advanced doctoral candidate in clinical psychology with 3 years of training in the headache treatment components.

Relaxation ratings were obtained at the end of each session containing PMR or cue-controlled relaxation. All participants received relaxation tapes for home practice relaxation. Additionally, patients receiving thermal biofeedback were instructed to practice at home with the aid of a small alcohol in glass thermometer given to them. Muscle tension and fingertip temperature were measured with electrodes (for muscle tension) and a thermistor (for temperature) supported by the MEDAC System/3 (Davicon; Billerica, MA) connected to an IBM PC.

All participants who received all treatment components sessions in the first phase of the study were considered treatment completers. After completing the first phase of the treatment, participants completed posttreatment forms, along with 2 weeks worth of headache medication and daily stress diaries. Scores from the BDI and PCL served as indicators of the presence of depression and posttraumatic stress. Being conservative, participants were offered treatment in the second portion of the study if they exhibited symptoms of depression and/or PTSD (based on scores of over 10 on the BDI and over 30 on the PCL) or had not significantly reduced headache activity by 50%.

The second phase of the treatment study targeted the PTSD and/or depression symptoms because the literature indicates these factors usually need to be addressed in order for headaches to improve. It was hoped that the cognitive therapy in the first phase would have alleviated associated symptoms; however, it was assumed that the posttraumatic stress symptoms would not be adequately addressed. Thus, this phase of treatment continued with cognitive therapy in addition to adding traditional exposure techniques. Some treatment components were drawn from a treatment study of MVA survivors by Blanchard et al. (2003). Cognitive therapy and relaxation carried over from Phase I of treatment. This treatment phase only lasted for six sessions (once a week for 4 weeks to allow adequate time for exposure homework and twice a week for the final week). The first three sessions focused on treatment of symptoms of posttraumatic stress and depression. Sessions 4–6 were similar to the first three, but included booster sessions of the headache treatment components. This second phase of the treatment study was offered to participants because it is assumed that the psychological symptoms, in particular posttraumatic stress symptoms, might have interfered with treatment response in the first phase of the study. Instead of incorporating these phases, the phases were separated because it was not expected that all participants would require the second treatment phase.

A between-group design was chosen for this study, instead of a multiple baseline design due to the potential difficulty of obtaining matched pairs in this sample. However, to the extent possible, participants were matched based first on headache features (i.e., tension, migraine, or mixed) and second on diagnosis of PTSD and/or depression. Half of the participants were assigned to a wait-list condition lasting as long as the first phase of the treatment (8 weeks that includes 2 weeks pretreatment).

RESULTS

Because there are so few controlled trials examining PTHA, we have been very liberal in reporting statistically significant results. For example, we have used one-tailed tests to compare treatment to wait list and pretreatment to posttreatment. We have also not applied a correction for the many analyses calculated on this small sample because we see this as more of an exploratory than confirmatory study.

Treatment Adequacy and Individual Participant Results

The average number of treatment sessions was 13.8 (range of 9–18). Overall, participants successfully learned to relax and control muscle tension and fingertip temperature. Average relaxation ratings by the end of treatment were 8.6 (on a scale of 0–10 where 10

indicates the deepest level of relaxation). In 90.4% of sessions, participants successfully decreased muscle tension; 87.6% of the time participants receiving thermal biofeedback increased temperature, with an average temperature during feedback of 92.2° F.

Because PTHA is an understudied disorder, we have presented the HA index results in Table I for each individual case. Four of the 14 participants experienced a positive clinically significant change in headache activity by the end of their last treatment session (improvement of 50% or greater). Six of the 14 participants showed some improvement (between 25 and 49%), 2 participants showed minor improvement (from 10 to 24%), and 2 participants experienced a worsening of symptoms based on posttreatment scores. A difference (though not significant) was found between percent improvement at the post and 2-month periods indicating that overall the participants showed further improvement at the 2-month follow-up, $t(11) = 0.66$, $p = .52$. Mean percent improvement at the posttreatment period was 25% (after completion of Phase I). By the 2-month follow-up mean percent improvement was 32%.

Between Group Results

To control for possible differences in groups at pretreatment, the posttreatment scores of HA index, medication index, and HA free days were compared in three separate analyses of covariance (ANCOVAs) with pretreatment scores as the covariate. The first ANCOVA examining HA index yielded a significant effect for the covariate, $F(1, 13) = 48.02$, $p < .001$, but no main effect of treatment condition, $F(1, 13) = 0.56$, $p = .471$. When comparing posttreatment HA free days in an ANCOVA using pretreatment values as the covariate, a significant effect was found for the covariate, $F(1, 13) = 7.07$, $p = .022$. Additionally, there was a main effect of treatment condition, $F(1, 13) = 4.95$, $p = .048$, indicating a significant difference posttreatment on number of HA free days between groups after controlling for pretreatment scores, with the treatment group having significantly more HA free days at postperiod compared to the wait-list group. Results from the third ANCOVA examining medication index scores yielded a significant effect for the covariate, $F(1, 13) = 155.27$, $p < .001$, but no main effect of treatment condition, $F(1, 13) = 0.014$, $p = .91$ (see Table II for HA and medication scores). Thus, the covariates were significant in all three ANCOVAs, indicating a strong relationship between pre- and post scores. However, controlling for pretreatment scores only resulted in a significant difference between treatment conditions on the number of HA free days but not HA or medication index scores.

Table II. Between Groups—Headache and Medication Scores

	Treatment group ($n = 7$)		Wait list ($n = 7$)	
	M	*SD*	*M*	*SD*
HA index				
Pre	5.0	3.2	8.0	4.8
Post	4.0	4.6	8.2	4.9
No. of HA free days				
Pre	4.7	4.0	1.0	2.2
post	6.1	4.4	0.6	1.1
Medication index				
Pre	4.4	6.1	2.3	2.8
Post	3.9	4.7	2.2	2.8

A one-tailed independent t test was conducted in order to compare percent improvement between the wait-list and treatment groups. These differences did not prove to be statistically significant, $t(13) = 1.09$, $p = .30$; however, mean improvement for the treatment group was 21%, whereas mean improvement for the wait-list group was −14% indicating a worsening of headache. Thus, although not significant, the treatment group showed arithmetically more improvement than the wait-list group.

Additional between-group comparisons (wait list vs. treatment) were made on the other treatment outcome measures (psychological tests). Separate analyses of covariance (ANCOVAs) were conducted using pretreatment scores as the covariate. No significant differences were found between groups on any of the psychological measures.

Within Group Results—Phase I

Within-group comparisons were conducted on all 14 of the PTHA participants based on pre- and posttreatment (Phase I) measures. Because one participant did not complete all posttreatment measures (HA and medication scores were calculated from the last 2 weeks of treatment) comparisons of pre- postpsychological measures were available for only 13 participants. Paired samples t tests (one-way) were used to analyze pre- to posttreatment scores for the entire sample. Additionally, paired samples t tests (one-way) were used to compare posttreatment to 2-month follow-up scores for all treated participants who returned 2-month follow-up data ($n = 12$).

Significant improvements were found in participants on HA index, $t(13) = 2.39$, $p < .05$. Headache activity decreased from pre- to posttreatment. The difference between the numbers of headache free days pre- to posttreatment was not statistically significant; however, increases in HA free days were seen from pre- to posttreatment. Medication intake was reduced significantly from pre- to posttreatment, $t(13) = 1.85$, $p < .05$. Comparison of post and 2-month scores (by participants who returned data at both points) did not show further improvement, however (see Table III for means and standard deviations).

Only one significant difference was found on the psychological measures when examining pre and postscores. Scores on the PCSC decreased from pretreatment, ($M = 78.5$, $SD = 21.2$) to posttreatment ($M = 61.2$, $SD = 13.2$) indicating an overall decrease in postconcussion symptoms, $t(12) = 3.69$, $p < .01$.

Table III. Within Groups—Pre, Post, and 2-Month Headache and Medication Scores

	Pretreatment		Posttreatment		2-month follow-up		
	M	*SD*	*M*	*SD*	*M*	*SD*	*t*[a]
$n = 14, df = 13$							
HA index	6.5	4.2	4.9	4.2	—	—	2.4*
No. of HA free days	2.9	3.7	4.6	4.7	—	—	−1.5
Medication index	3.4	4.7	2.6	4.0	—	—	1.9*
$n = 12, df = 11$							
HA index	5.7	3.2	4.3	4.0	4.1	3.6	−0.6
No. of HA free days	3.3	3.8	5.3	4.8	5.0	4.9	−0.3
Medication index	3.1	4.8	2.4	3.9	3.3	5.9	1.1

*$p < .05$, one tailed.
[a]The first set of t scores compare pre- to postscores; the second set compares post to 2-month.

When examining differences between the post and 2-month time periods, only scores on the STAI were significant. Participants showed decreases in State anxiety, $t(11) = -2.84$, $p = .016$, and Trait anxiety, $t(11) = -1.92$, $p = .05$, from the post (State: $M = 43.2$, $SD = 6.3$; Trait: $M = 46.8$, $SD = 8.5$) to 2-month (State: $M = 38.6$, $SD = 7.7$; Trait: $M = 42.5$, $SD = 7.0$) periods.

Phase II

Eleven participants were eligible for Phase II of treatment. Five participants completed Phase II, whereas three participants were unable to complete Phase II (due to accident and health problems) and three participants left Phase I early. Posttreatment scores were compared between eligible participants who completed Phase II and eligible participants who did not complete or start Phase II (scores used were posttreatment Phase II for completers and posttreatment Phase I for noncompleters). Again, for one participant who failed to return postmeasures only headache and medication data were available. One-tailed independent t tests were conducted in order to compare completers and noncompleters on headache, medication, and psychological measures. Only one statistically significant finding emerged on State Anxiety Scores, $t(8) = 4.58$, $p = .002$, indicating completers exhibited lower levels of state anxiety ($M = 38.8$, $SD = 1.3$) than noncompleters ($M = 48.0$, $SD = 4.3$).

DISCUSSION

Findings from this study indicate that psychological treatment for PTHA can be beneficial. Though the majority of differences were not statistically significant between the wait-list and immediate treatment groups, trends were in the expected direction for most measures. Overall, the treatment group did improve more than the wait-list group (+21% vs. −14%). The treatment group also showed a significantly greater improvement in headachefree days than the wait-list condition. Additionally, some other differences did approach statistical significance. A larger sample could increase power, leading to statistically significant differences.

The wait-list participants were crossed over and received treatment. When examining all treated participants on posttreatment measures, treatment appeared effective on reduction of the composite headache index measure and reduction of headache medications. However, not all measures indicated statistical significance. Overall, both headache and psychological distress tended to decrease with treatment. It was hoped that headache improvement would have been greater. By posttreatment, 29% of the sample (four people) showed clinically significant improvement (greater than 50% reduction in HA activity; moreover, another six participants (43%) showed some improvement (25–44%); however, by the 2-month follow-up only three people showed improvement of over 50%. Yet, these participants had headaches for a long time (5, 6, and 11 years). Eleven years was the longest time period of headache activity seen across participants and significant reduction in this participant's headaches (92% improvement) should not be discounted (see Table I for HA history information for all participants). In the posttreatment period mean improvement across all participants was 27%; 32% was the average headache improvement level seen by the 2-month follow-up. Because two participants failed to return data, it is possible that this percentage may be different.

Psychological symptoms decreased over time as well. Again, not all measures were significant from the pre- to postperiods, but overall arithmetic trends for a majority of the measures indicated improvement. Additionally, some scores were not necessarily in elevated ranges so change on these scores would not be as important in such cases.

As indicated by the number of participants who qualified for additional treatment after Phase I (11 of 14), this population needs a greater number of sessions than the "normal" headache population. This finding is consistent with previous studies suggesting the importance of additional sessions for PTHA patients (e.g., Hickling et al., 1992; Tsushima & Hawk, 1978). In some cases it might be argued that 18 sessions were still not enough especially with the multiple treatment components. However, those who completed the second phase tended to show slightly more improvement in HA relative to those who did not complete the second phase, further supporting the need for a greater number of treatment sessions in this population. One might argue that those who completed the second phase were less symptomatic to begin with and thus able to handle treatment requirements (compared to noncompleters who dropped out). However, comparing these two groups on preheadache index scores indicates no significant differences between completers and noncompleters.

A study where PTHA sufferers showed greater levels of improvement compared to this study had up to 50 treatment sessions (e.g., Hickling et al., 1992). It is possible that more sessions would have led to more HA reduction in this study; moreover, the participants in the current study presented with higher headache index scores compared to Hickling et al.' s sample. Because this treatment study was designed to address gaps in the research, its aim was to include an adequate number of sessions without individually tailoring the number of sessions in a way that might muddle results. Future studies should tackle this issue by examining how many sessions are adequate. Studies can accomplish this by varying number of treatment sessions offered and comparing groups based on number of sessions.

As mentioned previously in this paper, PTSD is an issue in PTHA. In fact prescores on the PCL were significantly positively correlated with pre-HA index scores, $r(12) = .64$, $p < .015$. With this in mind, did untreated PTSD influence response to treatment? To examine this question, scores on the PCL (total score) were compared across two groups (responders vs. nonresponders). Differences between groups based on independent samples t tests indicated treatment responders had lower PCL scores at pre- and post treatment (score at completion of treatment, which varied from participant to participant) compared to nonresponders; however, these differences were not significant. Pre- and post-PCL means for responders were 34.3 and 34.8, respectively, whereas nonresponders' means pre and post were 42.8 and 37.9, respectively. Thus, although responders had lower PCL scores at the start of treatment their mean scores did not change much after treatment. The nonresponders showed a decrease in symptoms by posttreatment (though not clinically meaningful).

As previously alluded to, a major limitation in this study was the sample size. Power analyzes conducted before the study started, based on the results of Hickling et al. (1992) indicated this sample size would be adequate; however, the present sample had more severe HA than the one on which the power analysis was based. A larger sample might have resulted in a greater number of statistically significant findings. Clearly future research should include larger samples.

A second reason for lack of significant findings might be due to the inclusion of people with different headache features. This study was designed to control for several factors and set up to administer a similar treatment to all participants, yet some of the

treatment was adjusted based on headache features. One solution would have been to obtain a greater number of subjects and compare people across headache types. Yet, difficulties in recruiting would have made this type of comparison problematic. Another solution would have been to limit the treatment to participants of one type of headache. This too would make it difficult to recruit the adequate sample size. Additionally, many of the PTHA participants had headache features that could fit along a headache continuum rather than then a specific headache type. One final solution would have been to give all participants the same treatment components, but it would be difficult to justify administering thermal biofeedback to participants with pure tension-type headaches, just as it would be difficult to justify not offering thermal biofeedback to those with migraines because thermal biofeedback is an empirically supported treatment for migraine headaches.

In conclusion, taking into account the limited sample size and exploratory nature of this study, the results were promising. This study confirmed the difficulties seen in treating the PTHA population. Though, it was hoped participants would show larger treatment gains, this study filled an important gap in the literature and highlighted the need for vigorous treatment in this underserved and frequently misunderstood population.

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Posttraumatic Headache: Biopsychosocial Comparisons With Multiple Control Groups

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Objective.—This study examined somatic, psychological, and cognitive functioning of subjects with posttraumatic headache in comparison with multiple control groups.

Background.—Posttraumatic headache is not as widely studied as other forms of headache (eg, tension-type, migraine). Previous research has suggested poor psychological functioning in patients with posttraumatic headache in comparison with other groups of patients with pain; however, this group has yet to be compared with a group of persons who have experienced trauma but are headache-free.

Design and Methods.—Nineteen subjects with posttraumatic headache were studied, with full assessments available for 14 participants. Comparison groups, containing 16 participants each, included another headache group, a nonheadache group, and a trauma (motor vehicle accident) survivor nonheadache group. Participants completed several measures assessing somatic, psychological, and cognitive functioning.

Results.—Findings revealed that the posttraumatic headache group exhibited significantly poorer functioning than the comparison groups on several measures including the Psychosomatic Symptom Checklist, Postconcussion Syndrome Checklist, axis II psychiatric diagnoses, Minnesota Multiphasic Personality Inventory, and the Daily Hassles Scale (frequency and total). Additionally, they scored higher on the following: number of axis I psychiatric diagnoses, the Daily Hassles Scale (intensity), Beck Depression Inventory, State-Trait Anxiety Inventory, and State-Trait Anger Expression Inventory. The posttraumatic headache group was similar to the other trauma group on the Posttraumatic Stress Disorder Symptom Checklist and the Life-Trauma Checklist.

Conclusions.—This study confirmed the distress seen in this understudied population of persons with headache and highlights areas of focus for proper assessment and treatment of those with headache and who have had an accident.

Key words: posttraumatic headaches, posttraumatic stress disorder, accidents

Abbreviations: PTHA posttraumatic headache, HA headache, PTSD posttraumatic stress disorder, MVA motor vehicle accident, MMPI Minnesota Multiphasic Personality Inventory, ANOVA analysis of variance

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Posttraumatic headache (PTHA) is usually one of a cluster of symptoms reported by patients after head trauma.[1] The symptoms can be categorized into 3 domains: somatic, psychological, and cognitive forming what is known as posthead trauma syndrome.[1] A brief review of these 3 areas will be outlined below before describing the current study.

Somatic.—Somatic symptoms associated with PTHA as part of the posthead trauma syndrome include, but are not limited to, dizziness, fatigue, nausea, weakness, insomnia, tinnitus, and visual disturbance.[2,3] Nausea, vomiting, and dizziness are the most common symptoms in the early phase of the head injury disturbance.[4] Longer-term physical complaints include

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insomnia, weight gain, muscle tenderness, and temporomandibular joint pain.[5] Patients with persisting symptoms are said to have posthead trauma syndrome.[4] These associated symptoms of head injury likely arise from both organic and functional causes.[6]

Psychological.—Studies point to the role of psychological difficulties in either contributing to or maintaining posttraumatic symptoms.[7-10] Additionally, psychological difficulties may develop after head injury, especially in cases where headaches (HAs) are an associated symptom.[11,12] Three main areas of study include personality, posttraumatic stress disorder (PTSD), and negative affect.

Personality is not typically implicated in the etiology of PTHA; however, premorbid personality may affect adjustment to injury and treatment outcome.[3] Research results on personality and PTHA are mixed. Studies have examined personality in this population beyond the typical personality changes seen in head injury (eg, irritability, mood swings). Patients with PTHA score significantly higher and often in the pathological range compared to patients with head injury without HA,[13] patients with other HA types (eg, migraine, tension-type, mixed, and cluster),[14-16] or patients with low back pain.[15] Other studies, however, have failed to find significant differences between PTHA and other HA groups on measures of personality.[17-19]

Diagnoses of PTSD in the PTHA population range from 29% to as high as 75%.[20-22] A considerable number of PTSD symptoms overlap with symptoms seen in the posthead trauma syndrome, including irritability, insomnia, anxiety, and memory difficulties. A treatment study by Hickling et al showed decreases in HA in this population when PTSD symptoms were addressed and reduced, making assessment and treatment of PTSD essential.[21]

Anxiety, depression, and anger are also common problems in the PTHA population.[20,23,24] When compared with other pain populations or control subjects, those with PTHA are found to have significantly higher levels of anxiety, depression, and anger.[5,15] These symptoms not only coexist, but they often interact with one another; for example, those with PTSD may report significantly higher levels of anger and depression.[20] Additionally, an examination of anger independent of PTSD revealed that anger suppression and expression directly affect depression in the PTHA population.[23]

Cognitive.—Across studies, persons who have experienced mild head trauma report cognitive disturbance, yet often these disturbances are difficult to detect.[25] General findings indicate a range of deficits including diminished rates of information processing, impaired problem-solving ability, mental fatigue, and disturbance of long-term and verbal memory.[26] In a study by Packard et al, 65 of 100 patients had cognitive difficulties, with problems or deficits in memory and concentration rated as the most prominent symptoms.[27]

Inconsistent findings across studies examining cognitive functioning may be due to measurement differences. Branca and colleagues found some differences on items of a subjective cognitive measure compared to an objective measure of cognitive functioning.[28] By way of contrast, an earlier study found that self-reported symptoms in patients with PTHA were highly associated with more impairment on objective tests.[29] Other factors, including the presence of anxiety or depression, can further complicate findings in studies of cognitive dysfunction.[25]

In a majority of studies, including those briefly mentioned above, patients with PTHA are compared to other HA populations or non-HA populations (or both). We believe the appropriate study of PTHA should include 3 comparison groups: (1) a population with chronic head pain not of traumatic origin, (2) a population who have suffered from traumatic events similar to those of the PTHA group but who do not have HA, and (3) an age- and sex-matched population who neither suffer from chronic HA nor who are survivors of a recent trauma. To the best of our knowledge, no study of PTHA has included all 3 of these comparison conditions. Since the majority of patients with PTHA develop their HAs secondary to motor vehicle accidents (MVAs), for comparison group 2 (trauma control) we have used a group of MVA survivors without HA. Thus, the purpose of this study was to examine functioning of a PTHA population across somatic, psychosocial, and cognitive domains in comparison with the complete set of controls described above. Based on the literature reviewed, it was estimated that the PTHA group would score significantly higher than all other groups on these measures.

METHODS

Subjects.—Persons with PTHA were recruited through several channels including a federally funded MVA survivor treatment study, a federally funded HA assessment study, physician referrals, and newspaper advertisements. Nineteen participants with PTHA were assessed as part of a separate treatment study. Five of these participants failed to finish the initial assessment, thus only partial data is available. Subjects with PTHA met the following criteria: their diagnosis (with or without confirmatory signs) was based on International Headache Society (IHS) criteria,[30] they had had HA for at least 6 months, they were 18 years of age or older, and they had been seen by a physician for their HA. Additionally, participants were diagnosed with migraine, tension-type, or mixed HA based on their HA features. The following exclusionary criteria applied: past or current psychotic symptoms, past or current manic symptoms, and current alcohol or substance abuse or dependence. A board-certified neurologist reviewed the HA interviews to corroborate diagnosis. Agreement of diagnosis occurred in all cases.

The study included the following control groups: 16 subjects with HA but not MVA, 16 healthy controls (no HA/no MVA), and 16 survivors of MVA trauma without HA. The HA/no MVA group was recruited through newspaper advertisements as part of a larger federally funded HA assessment study. These participants had received their choice of treatment or monetary compensation for completing a prior study. Additional monetary compensation was provided for participating in the current study. Participants were matched for age, gender, and HA type (tension-type, migraine, or mixed HA based on IHS criteria) to the PTHA group.[30]

A group of individuals involved in MVAs who did not develop HAs served as an accident comparison group (MVA/no HA). This group was recruited from a federally funded treatment study for persons who have had an accident. Participants received monetary compensation for taking part in the current study. These participants were matched for age and gender to the PTHA group.

A group of physically healthy HA-free participants served as a control group (no HA/no MVA). This group was also recruited through newspaper advertisements and received monetary compensation for participating. These participants were matched for age and gender to the PTHA group.

No differences emerged between groups on gender, age, race, socioeconomic status, education level, or marital status (Table 1).

Table 1.—Characteristics of Study Participants

Feature	Posttraumatic Headache Group (n = 19)	Headache/No Motor Vehicle Accident Group (n = 16)	No Headache/No Motor Vehicle Accident Group (n = 16)	Motor Vehicle Accident/No Headache Group (n = 16)
Sex, No.				
Males	4	2	3	5
Females	15	14	13	11
Age, mean (range), y	45 (23-82)	43 (21-70)	40 (18-73)	46 (26-71)
Race,%				
White	84	100	100	88
Hispanic	11			6
African American	5			
Other				6
Marital status,%				
Single	32	32	50	12.5
Married	37	56	44	44
Divorced	26	6	6	31
Widowed	5	6		12.5
Education, mean, y	15	16	16	14
Family income, mean, $	35 000	48 000	44 000	45 000

Procedures.—Eligible participants came to the clinic for an initial 3- to 4-hour assessment. Completion of all psychological tests occurred during or within 2 weeks of the initial evaluation. Somatic symptoms were assessed with the Psychosomatic Symptom Checklist and the Postconcussion Syndrome Checklist.[31,32] Psychological assessment instruments and tests included the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV Axis I Disorders (SCID-I),[33] Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II),[34] Minnesota Multiphasic Personality Inventory (MMPI) (original version), Daily Stress Inventory,[35] Daily Hassles Scale,[36] Beck Depression Inventory,[37] State-Trait Anxiety Inventory,[38] State-Trait Anger Expression Inventory,[39] Posttraumatic Stress Disorder Symptom Checklist (PCL-S),[40] and a Life-Trauma Checklist that served as an additional indicator of past trauma. To examine cognitive functioning, memory in particular, the Memory Assessment Scale was administered to all participants.[41]

RESULTS

Overview.—Between-group comparisons (PTHA versus HA/no MVA versus no HA/no MVA versus MVA/no HA) were made on all of the measures. It was expected that the PTHA group would evidence the poorest level of functioning, followed by the MVA/no HA group, then the HA/no MVA group, and finally, the no HA/no MVA group. One-way between-subjects analyses of variance (ANOVA) were used to examine differences. Corrections were not applied due to the small sample size and the desire to avoid type II errors.

Somatic.—Scores on the SUNY Symptom Checklist were significantly different between groups for the Frequency times Intensity (FI) score ($F_{3,59} = 15.22$; $P < .01$) and the total score ($F_{3,59} = 14.82$, $P < .01$). Results indicated that the PTHA group experienced significantly more functional symptoms than the other groups and the no HA/no MVA group experienced significantly fewer symptoms than the other groups. Means and standard deviations (SD) for the FI scores were as follows: PTHA: mean = 73.9, SD = 44.1; HA/no MVA: mean = 39.3, SD = 21.5; MVA/no HA: mean = 30.5, SD = 27.1; and no HA/no MVA: mean = 6.8, SD = 8.9. The total scores were: PTHA: mean = 10.1, SD = 4.2; HA/no MVA: mean = 7.8, SD = 3.3; MVA/no HA: mean = 5.6, SD = 2.9; and HA/no MVA: mean = 2.7, SD = 2.4.

The Postconcussion Syndrome Checklist total score was significantly different ($P = .01$) between groups ($F_{3,59} = 12.36$). The PTHA group scored significantly higher (mean = 81.9, SD = 22.4) than the other 3 groups and the no HA/no MVA group scored significantly lower (mean = 41.1, SD = 8.3) than the PTHA group and the other 2 control groups (HA/no MVA: mean = 56.6, SD = 19.6; MVA/no HA: mean = 57.1, SD = 21.6).

Psychological.—*Structured Interviews.*—Examination of the SCID-I revealed a significant difference on 1-way between-groups ANOVA for total number of axis I disorders ($F_{3,63} = 4.49$; $P < .01$). Post hoc tests revealed a significant difference between the no HA/no MVA group and the other 3 groups, indicating that those in the no HA/no MVA control group (mean = .1) endorsed less axis I pathology compared with the PTHA (mean = 1.5), MVA/no HA (mean = .9), and HA/no MVA (mean = .9) groups (see Table 2 for more specific information on axis I diagnoses). There were no significant differences in axis I pathology among the 3 other groups. Results from the SCID-II indicated significant differences between the PTHA group and the MVA/no HA and no HA/no MVA groups ($F_{3,60} = 3.78$; $P < .05$). A significantly higher number of axis II disorders were present in the PTHA group (mean = .6) compared with the MVA/no HA (mean = .1) and the no HA/no MVA (mean = 0) groups. The HA/no MVA group, with a mean of .3, was not significantly different from any of the groups (see Table 3 for more specific information on number of participants meeting axis II criteria based on the SCID-II).

Minnesota Multiphasic Personality Inventory.—One-way ANOVAs were conducted on the various MMPI standard scales and the following significant ($P \leq .05$ or .01) differences between the groups were found on the following scales: Infrequency, Hypochondriasis, Depression, Hysteria, Psychasthenia, Schizophrenia, Mania, and Social Introversion. For all scales with the exception of the Mania and Social Introversion scales, the PTHA group scored the highest, with mean T scores for

Table 2.—No. of Participants in Each Comparison Group With Axis I Diagnoses*

Diagnosis	Posttraumatic Headache Group (n = 19)	Headache/No Motor Vehicle Accident Group (n = 16)	No Headache/No Motor Vehicle Accident Group (n = 16)	Motor Vehicle Accident/No Headache Group (n = 16)
Major depression				
Current	7	0	0	4
Lifetime	12	7	1	10
Dysthymia	0	1	0	0
Depression NOS				
Current	0	0	0	0
Lifetime	0	0	2	0
Total No. of mood disorders				
Current	7	1	0	4
Lifetime	12	7	3	10
Agoraphobia without panic				
Current	0	0	0	0
Lifetime	0	0	0	0
Generalized anxiety disorder	5	2	1	1
Obsessive-compulsive disorder				
Current	0	0	0	0
Lifetime	1	0	0	1
Panic disorder				
Current	1	0	0	1
Lifetime	4	1	0	4
Posttraumatic stress disorder				
Current	8	1	0	5
Lifetime	11	5	0	13
Social phobia				
Current	3	3	0	0
Lifetime	4	3	0	1
Specific phobia				
Current	4	4	0	1
Lifetime	4	4	0	1
Total No. of anxiety disorders				
Current	21	10	1	8
Lifetime	24	13	0	20
Substance-related disorders				
Current	0	0	0	1
Lifetime				
Abuse	1	0	2	2
Dependence	2	0	1	2
Somatization disorder	1	1	0	2
Eating disorder				
Current	0	3	0	0
Lifetime	3	5	0	1
Total No. of axis I disorders				
Current	37	15	1	15
Lifetime	42	25	6	35

*NOS indicates not otherwise specified.

half of these scales over 70, indicating clinically meaningful problems. When examining statistically significant scores, several patterns emerged. On the Infrequency, Depression, and Psychasthenia scales, the no HA/no MVA group scored significantly lower than the other 3 groups. There were no significant differences among the other 3 groups on these 3 scales. On the Hypochondriasis scale, the no HA/no MVA group scored significantly lower than the other 3 groups. Additionally, the PTHA group scored significantly higher

Table 3.—No. of Participants in Each Comparison Group With Axis II Diagnoses

Type of Personality Disorder	Posttraumatic Headache Group (n = 16)	Headache/No Motor Vehicle Accident Group (n = 16)	No Headache/No Motor Vehicle Accident Group (n = 16)	Motor Vehicle Accident/No Headache Group (n = 16)
Paranoid	0	0	0	1
Schizoid	0	0	0	0
Schizotypal	0	0	0	0
Antisocial	0	0	0	0
Borderline	2	0	0	0
Histrionic	0	0	0	0
Narcissistic	0	0	0	0
Avoidant	2	3	0	1
Dependent	1	0	0	0
Obsessive-compulsive	4	1	0	0
Any axis II disorder	9	4	0	2

than the MVA/no HA group. However, the HA/no MVA group's Hypochondriasis scores were not significantly different from either the PTHA or MVA/no HA groups. For the Hysteria scale, post hoc tests revealed that the PTHA group scored significantly higher than the 3 control groups. In addition, the no HA/no MVA group scored significantly lower than the other 3 groups. Scores from the Schizophrenia scale revealed significant differences between the no HA/no MVA group and both the PTHA and MVA/no HA groups, with the no HA/no MVA group scoring lower. No other differences emerged between groups on the Schizophrenia scale. On the Mania scale, the MVA/no HA group scored significantly higher than the other 3 groups. The other 3 groups did not score significantly different on the Mania scale. Finally, on the Social Introversion scale, the no HA/no MVA group scored significantly lower than the 2 HA groups and the MVA/no HA group also scored significantly lower than the HA/no MVA group. No other differences were found on this scale. (See Table 4 for results of all MMPI scales.)

Life Stress.—Participants completed 2 weeks of Daily Stress Inventories. An average of weekly Impact/Event scores was used in the analysis. The Daily Stress Impact/Event ratio T scores were significantly different between groups ($F_{3,58} = 3.87$; $P < .05$). The 2 HA groups had T scores that were higher than the 2 no HA groups (as shown in Table 5) indicating that stressors are perceived to have a greater impact in the HA groups compared to the no HA groups. Even so, only the HA/no MVA group scored significantly higher than the 2 no HA groups. The PTHA group scored significantly higher than the no HA/no MVA group, but not the MVA/no HA group.

Significant differences were found among groups on all 3 scores of the Daily Hassles Scale: Frequency ($F_{3,59} = 12.70$; $P < .01$), Total ($F_{3,59} = 10.37$; $P < .01$), and Intensity ($F_{3,59} = 4.89$; $P < .01$). With 2 of these scores (Frequency and Total), the PTHA group scored significantly higher than the rest, and the no HA/no MVA group scored significantly lower than the rest. A different pattern emerged on the Intensity score, however. The PTHA and HA/no MVA groups only scored significantly higher than the no HA/no MVA group; thus, although these 2 groups may endorse a significantly different number of events, they do not experience them at significantly different levels of intensity (as shown in Table 5).

Results from the Beck Depression Inventory indicated a significant difference between groups ($F_{3,60} = 6.10$; $P < .01$). The no HA/no MVA group endorsed fewer items on the Inventory compared with the PTHA, HA/no MVA, and MVA/no HA groups who did not differ. Scores for these 3 groups indicate mild depression (Table 6).

Table 4.—Comparison of Study Participant Groups on Minnesota Multiphasic Personality Inventory Standard Scale Scores*

Scale	Posttraumatic Headache Group	Headache/No Motor Vehicle Accident Group	No Headache/No Motor Vehicle Accident Group	Motor Vehicle Accident/No Headache Group	$F_{3,59}$ Score
Lie	53.6 (10.5)	52.0 (8.4)	54.6 (10.2)	52.7 (5.6)	.3
Infrequency	63.5 (12.0)§	58.4 (7.8)§	50.9 (6.4)‖	60.6 (11.4)§	4.9†
Defensiveness	53.6 (11.4)	56.3 (9.0)	62.1 (10.3)	55.3 (10.3)	2.0
Hypochondriasis	75.9 (18.2)§	67.8 (14.2)§,‖	50.3 (5.1)¶	64.1 (15.5)‖	9.1†
Depression	77.3 (18.4)§	73.8 (16.2)§	52.9 (7.5)‖	68.4 (21.0)§	6.7†
Hysteria	76.4 (15.3)§	67.8 (12.6)‖	56.0 (7.1)¶	64.6 (11.3)‖	7.8†
Psychopathic deviate	68.4 (14.0)	60.5 (8.8)	58.8 (7.9)	66.3 (14.1)	2.5
Masculinity-femininity	50.9 (9.4)	46.4 (11.4)	52.4 (12.7)	52.9 (7.7)	1.3
Paranoia	61.1 (9.8)	63.9 (8.8)	55.6 (4.9)	62.4 (12.8)	2.3
Psychasthenia	64.5 (11.7)§	64.4 (8.1)§	52.6 (5.4)‖	63.0 (15.5)§	4.5†
Schizophrenia	71.1 (15.7)§	62.1 (9.6)§,‖	55.7 (5.1)‖	66.7 (17.7)§	4.0‡
Mania	51.9 (10.0)§	47.8 (8.4)§	53.4 (10.4)§	61.0 (10.9)‖	4.9†
Social introversion	60.5 (11.5)§,‖	63.9 (10.2)§	50.6 (10.9)¶	55.7 (11.8)‖,¶	4.3†

*Values are means (SD).
†$P \leq .01$.
‡$P \leq .05$.
§,‖,¶Group means that share one of these superscripts do not differ at the .05 level.

Examination of the State-Trait Anxiety Inventory revealed significant differences between groups on both the State Anxiety ($F_{3,59} = 9.27$; $P < .01$) and Trait Anxiety ($F_{3,59} = 6.59$; $P < .01$) scores (Table 6). Again, similar to Beck Depression scores, the no HA/no MVA group scored significantly lower on both the State and Trait scores compared to the other 3 groups that did not differ significantly.

No significant differences were found between groups on the State-Trait Anger Expression Inventory (Table 6).

One-way between-groups ANOVA revealed significant differences between the 4 groups on the Life-Trauma Checklist ($F_{3,61} = 9.15$; $P < .01$). The PTHA group and MVA/no HA group experienced a significantly greater number of traumatic life events

Table 5.—Comparison of Study Participant Groups on the Daily Hassles Scale and Daily Stress Inventory Scores*

Scale	Posttraumatic Headache Group	Headache/No Motor Vehicle Accident Group	No Headache/No Motor Vehicle Accident Group	Motor Vehicle Accident/No Headache Group	F Score
Daily Hassles Scale					$df = 59$
Frequency	62.5 (15.9)§	47.6 (18.7)‖	21.9 (15.1)¶	46.9 (23.5)‖	12.7†
Intensity	1.7 (.4)§	1.6 (.3)§	1.2 (.4)‖	1.4 (.4)§,‖	4.9†
Total	109.1 (40.9)§	73.9 (31.6)‖	30.5 (27.6)¶	73.8 (52.8)‖	10.4†
Daily Stress Inventory					$df = 58$
Impact/event ratio T score	56.0 (12.3)§,‖	58.1 (7.7)§	46.3 (.8)¶	49.8 (14.1)‖,¶	3.9‡

*Values are means (SD).
†$P \leq .01$.
‡$P \leq .05$.
§,‖,¶Group means that share one of these superscripts do not differ at the .05 level.

Table 6.—Comparison of Study Participant Groups on the Beck Depression Inventory and the State-Trait Anxiety and Anger Expression Inventories*

Inventory	Posttraumatic Headache Group	Headache/No Motor Vehicle Accident Group	No Headache/No Motor Vehicle Accident Group	Motor Vehicle Accident/No Headache Group	$F_{3,62}$ Score
Beck Depression Inventory	15.4 (11.9)‡	11.8 (5.2)‡	2.9 (4.1)§	12.1 (10.6)‡	6.1†
State-Trait Anxiety Inventory					
State Anxiety	48.1 (14.5)‡	43.2 (9.6)‡	27.9 (8.6)§	40.1 (11.6)‡	9.3†
Trait Anxiety	48.8 (13.0)‡	46.9 (9.7)‡	32.3 (9.0)§	41.9 (13.6)‡	6.6†
State-Trait Anger Expression Inventory					
State Anger T score	55.1 (7.4)	51.9 (4.9)	51.6 (3.1)	55.0 (8.1)	1.5
Trait Anger T score	49.3 (11.4)	40.2 (9.8)	46.3 (8.5)	42.4 (14.7)	2.0

*Values are means (SD).
†$P \leq .01$.
‡,§Group means that share one of these superscripts do not differ at the .05 level.

(mean = 5.4 for both groups) compared with the HA/no MVA (mean = 2.5) and no HA/no MVA groups (mean = 2.3). Even so, there were no differences between the groups for number of traumatic events witnessed or learned about.

Examination of scores on the Posttraumatic Stress Disorder Symptom Checklist revealed significant differences between the groups on Cluster C symptoms ($F_{3,60} = 9.98$; $P < .01$), Cluster D symptoms ($F_{3,60} = 9.90$; $P < .01$), and total score ($F_{3,60} = 8.47$; $P < .01$); however, there was not a significant difference between the groups on Cluster B (re-experiencing symptoms). Those in the PTHA and MVA/no HA groups endorsed significantly more symptoms of PTSD compared to the other 2 groups (as shown in Table 7). In turn, the PTHA and MVA/no HA groups did not differ nor did the HA/no MVA and no HA/no MVA groups.

Cognitive.—Results from 1-way between-groups ANOVA indicated one significant difference on the Short-term Memory Full Scale score of the Memory Assessment Scale ($F_{3,62} = 3.88$; $P < .05$). Post hoc tests revealed significant differences between the no HA/no MVA group and 2 other groups, the HA/no MVA and MVA/no HA groups. The average score for the PTHA group was not significantly different from the other 3 groups. No differences emerged on Global Memory, Visual Memory, or Verbal Memory (Table 8).

COMMENTS

There are 3 different groups with whom patients with PTHA should be compared: those with HA not of

Table 7.—Comparison of Study Participant Groups on the Posttraumatic Stress Disorder Symptom Checklist-S*

Cluster Symptoms	Posttraumatic Headache Group	Headache/No Motor Vehicle Accident Group	No Headache/No Motor Vehicle Accident Group	Motor Vehicle Accident/No Headache Group	$F_{3,60}$ Score
Cluster B	10.5 (4.5)	7.4 (3.2)	8.3 (4.7)	8.2 (3.5)	1.8
Cluster C	18.0 (6.5)‡	8.9 (4.9)§	8.9 (2.7)§	14.9 (7.5)‡	10.0†
Cluster D	13.8 (4.9)‡	6.6 (3.5)§	7.0 (3.7)§	12.1 (5.8)‡	9.9†
Total score	42.3 (14.6)‡	22.9 (11.0)§	24.3 (9.9)§	35.2 (14.6)‡	8.5†

*Values are means (SD).
†$P \leq .01$.
‡,§Group means that share one of these superscripts do not differ at the .05 level.

Table 8.—Comparison of Study Participant Groups on the Memory Assessment Scale*

Memory Full Scale Score	Posttraumatic Headache Group	Headache/No Motor Vehicle Accident Group	No Headache/No Motor Vehicle Accident Group	Motor Vehicle Accident/No Headache Group	$F_{3,62}$ Score
Short-term	95.6 (12.2)†,§	88.9 (12.8)‡	101.0 (10.3)§	88.8 (12.7)‡	3.9†
Visual	92.6 (17.9)	84.8 (12.5)	94.3 (11.6)	89.9 (14.7)	1.3
Verbal	91.1 (12.9)	94.5 (11.9)	95.4 (13.0)	94.9 (11.4)	.4
Global	90.4 (17.0)	87.9 (13.2)	93.5 (12.3)	91.1 (13.2)	.4

*Values are means (SD).
†$P < .05$.
‡,§Group means that share one of these superscripts do not differ at the .05 level.

a posttraumatic origin (HA/no MVA), those who have experienced a traumatic injury, but do not report HAs (MVA/no HA), and a control group who neither have HAs nor have suffered from a traumatic injury (no HA/no MVA). To the best of our knowledge, no prior study prior has simultaneously compared patients with PTHA with all 3 groups.

On measures of physical symptoms, our PTHA group tended to report physical difficulties in addition to their HAs. These comorbid physical problems may affect psychological functioning and, to some degree, explain other differences recorded between those in the PTHA group and the other groups.

The PTHA group experienced more psychological distress, including more axis I and II pathology. On several MMPI scales, the PTHA group scored the highest; the most notable elevated scores were on the "neurotic triad" scales (Depression, Hypochondriasis, and Hysteria), with means for the PTHA group above 75, and the participants with PTHA also had the highest clinically significant score on the Schizophrenia scale. Though there are mixed results in the literature regarding personality inventories of PTHA versus other populations, our findings are consistent with those of others.[13,14] Generally, the no HA/no MVA control group showed the least psychic distress compared to the other 3 groups.

It may be hypothesized that a diagnosis of PTSD may influence the MMPI scores in the PTHA group, but when the relationship between PTSD and MMPI scores was examined, there was only one significant difference between participants with PTHA with (n = 6) or without (n = 8) PTSD (based on the SCID-I): the Paranoia scale. Although other statistically significant differences were found, across several of the scales (ie, Depression, Hyphochondriasis, Hysteria, Psychopathic Deviate, Psychasthenia, Schizophrenia, and Social Introversion), the participants with PTHA and PTSD scored higher than those without a diagnosis of PTSD. There is, thus, a possible connection between PTSD and elevated MMPI scores.

When we examined other psychological measures, similar patterns emerged. Daily life stress was also more prevalent in those with PTHA, and again, the no HA/no MVA group reported the least amount of stress. The HA/no MVA and MVA/no HA groups generally showed similar levels of stress, but one interesting discrepancy emerged: the PTHA group was experiencing more stress, but results differed depending on time of evaluation. For retrospective ratings (ie, the Daily Hassles Scale), the PTHA group scored higher than the other groups, but for prospective daily stressor measurements (ie, Daily Stress Inventory), the PTHA group perceived stressful events at levels similar to the HA/no MVA and MVA/no HA groups.

On measures of depression and anxiety, the PTHA group scored significantly higher than the other 3 groups. These results are in line with results from the SCID interview. Surprisingly, while state and trait anger were also higher, the results were not significant. Once again, the no HA/no MVA controls showed the least symptoms of depression and anxiety with the HA/no MVA and MVA/no HA groups falling between the PTHA and no HA/no MVA groups.

As for current posttrauma symptoms, both the PTHA and MVA/no HA groups scored significantly higher on the PTSD Checklist; a result to be expected due to the presence of past trauma that defined these groups. These trauma groups also reported higher levels of other past trauma, but there was not a significant difference among the groups on Cluster B (re-experiencing) symptoms. Some of the other PTSD symptoms endorsed may have reflected underlying depression or posthead trauma syndrome and not actual PTSD. These results speak to the difficulty of distinguishing PTSD symptoms from other related problems (eg, depression, cognitive difficulties, anxiety) that are common in this population.

On the memory test, all groups scored in the normal range of functioning. Despite a greater amount of endorsement of memory problems by the PTHA group based on a clinical interview (where 100% of those with PTHA reported at least one cognitive symptom), the objective measure (ie, Memory Assessment Scale) did not indicate significant differences. In fact, on the Global Memory score, the HA/no MVA group had the lowest mean score, and on the Short-term and Visual Memory scores, the HA/no MVA and MVA/no HA groups both scored means lower than that of the PTHA group. It is possible that perceived memory problems may be related to subtle organic abnormalities present in patients with PTHA symptoms related to mild head injury.[42] Tests beyond the scope of this study, such as cognitive evoked potentials, might have been useful in addition to subjective self-report and memory testing.

Two qualifications regarding the results must be made. First, as previously noted, despite the large number of measures administered, corrections were not applied. As this was an exploratory study with a small sample size, this approach was taken in order to avoid type II errors. It may be possible that some of the significant findings are based on chance. Even so, the results are strengthened since across the majority of the measures, even if not statistically significant, the PTHA group shows the highest levels of distress.

Secondly, recruitment procedures may have influenced the results. Some of the participants in this study were drawn from other clinical samples, thus possibly skewing the results. The PTHA and MVA/no HA groups were both recruited to participate in treatment studies and the HA/no MVA group was offered treatment as an option for participating in the larger study from which they were drawn. These groups may be different from other HA and accident populations that do not seek psychological treatment.

Nonetheless, the findings from this study indicate a higher level of distress along many dimensions in those with PTHA compared with the other 3 groups tested. Those with PTHA have more psychological distress and may experience stress at a higher intensity. This supports many previous studies.[14-16,21,22] These findings may explain why this HA group is more refractory to treatment. Our results, however, did not conclusively support the hypothesis that the MVA/no HA group experiences higher psychological distress than the HA/no MVA group. Except for trauma, general psychological distress typically was similar in these populations.

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In Press: Behavioral Medicine

Activity and sleep contribute to levels of anticipatory distress in breast surgery patients.

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Running Head: ACTIVITY AND SLEEP IN BREAST SURGERY PATIENTS

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Abstract

A high level of anticipatory distress in women scheduled for surgery to detect/treat breast cancer makes the need for investigation of potential targets for distress reducing interventions of paramount importance. Exercise and sleep have been examined in relation to distress in this population, focusing on the post-surgery period. This study examined the contributions of physical activity and sleep to anticipatory distress levels in 124 women prior to breast surgery. Patients completed measures of distress, activity and sleep. It was expected that higher levels of activity and better sleep would be associated with lower anticipatory distress. Additionally, it was expected that the effects of physical activity on distress would be accounted for by (mediated) sleep quality. Results indicated that physical activity and sleep quality were negatively related to distress ($p < .05$); however, activity effects were not mediated by sleep. These findings have implications for designing interventions to reduce anticipatory breast-surgery distress.

Index Terms: breast cancer, anticipatory distress, sleep, activity

Activity and sleep contribute to levels of anticipatory distress in breast surgery patients.

Breast cancer is one of the most commonly diagnosed cancers among women in the United States.[1] Women scheduled for either curative or diagnostic breast surgery, to remove suspicious or cancerous tissue, experience high degrees of anticipatory distress prior to undergoing surgical procedures.[2-6] With several hundred thousand women undergoing diagnostic procedures each year and over 150,000 lumpectomies and mastectomies performed annually[7], research examining possible areas of intervention for reducing anticipatory distress are of paramount importance. Research studies conducted in the exercise and sleep realms suggest these are two possible factors linked to distress that could serve as possible intervention foci. While both exercise and sleep have been studied in breast cancer patients in the post-surgery period, information regarding their effects prior to surgery is lacking. The literature on distress and exercise, distress and sleep and the exercise-sleep connection are outlined below, along with a discussion of the research in these areas with breast cancer populations.

Distress and Exercise

Exercise is one potential intervention focus that could result in reduction of anticipatory distress. The relationships between exercise and psychological factors including distress have been studied extensively with over 100 published reviews in this area.[8-10] Due to variability in populations and study methods, drawing definitive conclusions can be difficult. However, based on meta-analyses examining exercise intervention effects on distress (e.g., depression[11-13] and anxiety[14]), it appears that exercise, whether acute or long term, has the strong potential for alleviating distress.

The effects of exercise on distress prior to surgical procedures, in particular breast surgery, are as yet not clearly defined.

Distress and Sleep

Sleep may be another intervention domain to target, especially since disturbed sleep can negatively impact distress levels. Poor sleep quality has been associated with distress in a variety of healthy female populations.[15-18] Rate of poor sleep and distress levels are likely to be higher in non-healthy women. For example, a study by Shaver[19] and associates compared women with fibromyalgia to a healthy comparison subjects and found that the healthy women reported better sleep quality as well as less distress. As with the exercise literature, the sleep literature has not examined the effects of sleep on distress levels prior to surgery to our knowledge.

Exercise and Sleep

It seems intuitive that exercise and sleep would be positively related; however, the relationship between exercise and sleep has been debated for several years. An early extensive review by Horne[20] discussed methodological problems in the exercise-sleep literature that make many conclusions tenuous. First, studies examining the effects of regular exercise on sleep were lacking in the literature. Second, potentially beneficial subjective measures of sleep quality and quantity were not frequently utilized. Many of these problems still exist in the literature today.

Despite these debates, accumulating evidence suggests a positive connection between exercise and sleep. Baekeland[21] reported negative effects on sleep in fit subjects who were prohibited from exercising. Conversely, higher levels of fitness are associated with better sleep.[22-24] Results from large scale studies support the benefits of exercise on

sleep.[25-31] Additionally, a meta-analysis revealed that even acute exercise may have some benefits on sleep.[32] Furthermore, studies have found beneficial effects of exercise on sleep in people with sleep difficulties.[33-36]

Exercise, Sleep and Breast Cancer

Both exercise and sleep are areas that have been explored in breast cancer populations. A small number of studies examined the positive effects of exercise on symptoms (both physical and/or psychological) in breast cancer patients.[37-45] While two-thirds of these studies examined distress in addition to physical symptoms such as fatigue, none have studied the role of exercise in reducing distress *prior* to surgery. Instead, all of these studies focused on the effects of exercise post-treatment (on average one year post-surgery/treatment). The study of sleep in cancer patients has focused on the development of sleep disorders during the post-treatment period. This focus is surprising as it has been reported that 48% of insomnia cases in cancer patients occur around the time of diagnosis; with distress being a significant contributor.[46] In general, studies have yet to examine how sleep prior to surgery may influence anticipatory distress levels.

In summary, previous studies suggest the likely relationship between exercise, sleep and distress. Therefore, it appears that exploring the effects of exercise and sleep on anticipatory distress in women scheduled for breast surgery could potentially lead to the development of new or enhanced interventions to reduce pre-surgical distress.

We propose the following three hypotheses 1) Women with higher levels of physical activity prior to surgery will have lower distress levels; 2) Better sleep will be associated with lower levels of distress; and, 3) The effects of physical activity on

distress prior to surgery will be accounted for (mediated) by sleep quality. These hypotheses will be tested in a sample of breast cancer surgery patients where heightened levels of distress prior to surgery have been demonstrated in the literature.

Method

Participants

The sample consisted of 124 females undergoing excisional breast biopsy or lumpectomy. From the surgical perspective, there is little difference between these procedures.[47] Mastectomy patients were excluded as their surgical and anesthesia procedures are markedly different. Participants, referred by their breast surgeon, were recruited following surgical consultation. All participants provided informed consent according to the guidelines of the Mount Sinai School of Medicine Institutional Review Board. In order to participate, patients had to be English speakers, over age 18 and not in psychiatric treatment for mental illness.

Age ranged from 19 to 77 years (mean age = 48.3, SD = 12.7). Seventy three point nine percent of the sample described themselves as white, 8.1% as African American, and 12.6% Hispanic. Fifty-three percent of the sample was married and 42.3% had a standard college education. Ninety six participants underwent excisional biopsies, while 28 had lumpectomies.

Measures and Procedures

In the clinic waiting area, on the day of surgery, participants completed a questionnaire assessing activity, sleep and distress. The outcome variable, distress, was measured with the Profile of Mood States-Short Version (SV-POMS). The SV-POMS provides an overall mood score for the past week plus six subscale scores, and is a

shortened version[48] of the original POMS.[49] This shortened version, while less burdensome has been demonstrated to be reliable with breast cancer patients.[48]

In consideration of patient burden, brief measures were used to assess the predictors. Two items were used to assess sleep and one to assess activity. The first sleep question was extracted from the Functional Assessment of Cancer Therapy - Fatigue (FACT-F, version 4), a reliable and valid measure of quality of life in cancer patients with a focus on fatigue.[50] This question measuring sleep quality for the past week, reads as follows: "I am sleeping well," and is rated on a 0 to 4 scale where 0 indicates "not at all" to 4 indicating "very much". A similar sleep quality measure was used successfully by Moore and colleagues.[51] Even though sleep quality may relate better to measures of distress than sleep quantity,[52] the sleep deprivation literature indicates that even one night of sleep loss can have significant negative effects on mood.[53] Therefore, in addition to sleep quality, we decided to also gather information on the number of hours of sleep on the night before surgery to determine whether the previous night's sleep quantity affected distress.

The activity question of interest, developed for this study, asks: "In the past week, how many times did you engage in an activity long enough to work up a sweat, get the heart thumping, or get out of breath?" The purpose of this item was to capture all forms of strenuous physical activity, not only those identified specifically as "exercise". Use of such self-report approaches to measure physical activity has been found to be both valid and reliable,[54] while limiting additional patient burden.

The following three hypotheses were tested: 1) Women with higher levels of physical activity will have lower distress levels prior to surgery; 2) Better quality sleep

will be associated with lower levels of distress prior to surgery; and, 3) Sleep quality will account for the relation between (mediate) activity and anticipatory distress.

Results

Neither demographic variables, body mass index (BMI) nor type of surgery (excisional breast biopsy vs. lumpectomy) contributed to distress (p's>.10), and therefore were dropped from further analyses.

Due to lack of normality for the activity item distribution (skewness = 1.54; kurtosis=5.79), the sample was divided into two groups reflecting regularity of activity; a no/low activity group (those who engaged in activity 0-1 time over the week before surgery) and a high activity group (those who engaged in activity 2 or more times in the week before surgery).

(Insert Figure 1 about here)

Patients in the high activity group had significantly greater distress [t (122) = 1.93; p=.05] compared to the no/low activity group (see Figure 1). Predicted values (based on the regression equation) of SV-POMS by sleep quality scores are displayed in Figure 2. As presented in Figure 2, SV-POMS scores got progressively lower as sleep quality ratings got higher, indicating better sleep quality.

(Insert Figure 2 about here)

Both bivariate and multivariate correlations between the predictors and distress prior to surgery are presented in Figure 3.

(Insert Figure 3 about here)

To establish sleep as a mediator of the effects of activity on distress, three regression analyses were performed according to published criteria.[55] First, we examined

the correlation between the hypothesized mediator (sleep) and the independent variable (activity). Although sleep quality over the past week was of primary interested, as previously discussed, we also included sleep quantity (last night) in the analysis to control for the influence of this factor. Results indicated that activity was significantly correlated with sleep quantity ($p = .01$), but not sleep quality ($p > .10$). Therefore, data were consistent with the possibility that sleep quantity, but not sleep quality, accounted for the effects of activity on anticipatory distress according to Criterion 1. To test Criterion 2, we examined the correlation between the dependent variable (distress, as measure by SV-POMS) and the independent variable (activity). The correlation between activity and distress was significant ($p= .05$) in bivariate analyses. To examine Criterion 3, we conducted simultaneous regression analyses with activity and sleep serving as predictor variables and the outcome variable being patients' distress prior to surgery (see Figure 1). Activity [$F (1,120) = 4.90$; $p= .03$] and sleep quality [$F (1,120) = 29.04$; $p= .01$] each made significant unique contributions to distress level as measured by the SV-POMS, inconsistent with mediation. Examination of sleep quantity indicated that the variable did not contribute [$F (1,120) = 1.54$; $p>.20$] in this simultaneous regression model. Together activity and sleep quality accounted for 22% of the variance in anticipatory distress. Thus, it appears that activity and sleep quality were each independently associated with patients' anticipatory distress.

Since sleep did not serve as a mediator, it is appropriate to examine the possible synergistic effect of activity and sleep quality on distress (total SV-POMS). To address this possibility, a simultaneous regression analysis with three predictors (activity, sleep quality and the interaction of activity by sleep quality) was performed. The interaction

between activity and sleep quality was not significant [F (1,120) = 1.12; p >.10], indicating that there was no significant difference in the effect of sleep quality on distress for those who engage in more physical activity versus those who engage in less physical activity.

As our distress measure was comprised of six validated subscales, it was of interest to determine whether sleep quality and activity contributed differentially to the specific SV-POMS subscales. Thus, we performed separate simultaneous regression analyses for each of the six SV-POMS subscales (see Table 1). Sleep quality was significantly associated ($p < .01$) with all of the SV-POMS subscales except for Vigor. However, activity was only associated with fatigue and confusion ($p < .05$). The interaction between sleep quality and activity was significant only for the Confusion subscale ($p = .04$), indicating that those with a high level of activity and better sleep quality reported less confusion.

To control for the possibility that distress on the day of surgery could influence retrospective ratings for sleep and distress over the past week, we used a visual analogue scale (VAS) measuring level of upset on day of surgery as a covariate in our regression original model. After controlling for distress on day of surgery, activity [F (1,120) = 5.48; $p = .02$] and sleep quality [F (1,120) = 19.85; $p = .01$] both continued to make significant contributions to anticipatory distress level. Again, sleep quantity did not contribute in this simultaneous regression model [F (1,120) = 2.49; $p > .10$].

Comment

Hypotheses 1 and 2 were supported; Hypothesis 3 was not. Consistent with hypothesis 1, women with higher levels of physical activity had lower distress levels

prior to surgery. Additionally, better sleep was associated with lower levels of distress prior to surgery (hypothesis 2). Interestingly, sleep quantity was not significantly associated with distress. Taken together it appears that the perception of sleep quality, rather than the actual quantity of hours of sleep, contributed to anticipatory distress. Indeed, as previously discussed, sleep quality was more likely to be related to distress as compared to quantity.[52]

Surprisingly, sleep quality did not serve as a mediator between activity and anticipatory distress. That is, sleep did not account for the effects of activity on distress. Additionally, there was also no synergy between sleep quality and activity. We had speculated that those that both exercised more and slept better would have the least anticipatory distress. This was not the case. Each factor contributed as a main effect, but the interaction was not significant. Further SV-POMS subscale analyses revealed a broad effect of sleep quality on specific mood states. It appears that sleep quality has a widespread effect on mood with better sleep quality correlating with less distress, while activity exerts potentially more specific effects on fatigue and confusion only.

An important contribution of this study to the literature is the examination of the effects of activity and sleep on distress prior to surgery, rather than after surgery. Future studies, however, might want to examine these variables in different contexts that were beyond the scope of this current study. For example, women with breast cancer are at generally at greater risk for developing insomnia.[56] An examination of the influence of distress on sleep could illuminate additional areas to target in breast cancer patients facing the threat of surgery.

This study is not without its limitations. First, the current study is correlational in design and causality cannot be assumed. Nevertheless, the study documents the associations among activity, sleep quality and anticipatory distress for the first time in the breast cancer literature. A second limitation of the study is that the activity measure only captured one week of activity prior to surgery. It is quite possible that activity during the week prior to surgery might be markedly different from a "normal" week, and activity level might not be fully captured. Yet, studies have found even acute exercise influences distress,[14] thus activity in the week prior to surgery might be especially crucial for relieving distress. It might also be possible that fitness level, rather than activity may be influencing distress. However, examination of BMI, a relatively stable measure associated with fitness level,[57-58] revealed no connection between fitness and distress. Lastly, patients were recruited from one of two surgeons, thus generalizability to other surgeons must be established. However, the diversity of our sample population in both ethnicity and economic background may allow for broader application of the present findings. Additionally, the mean anticipatory distress scores from this sample are comparable to other breast treatment/surgery populations.[48,59]

These results suggest that activity and good sleep may act as buffers against distress associated with breast cancer surgery. Indeed, these data support the view that interventions to increase activity and improve sleep quality may help reduce anticipatory distress. As activity and sleep are also easily identified intervention targets, an empirical test of such interventions seems warranted.

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Figure 1. Mean SV-POMS score by Activity Group

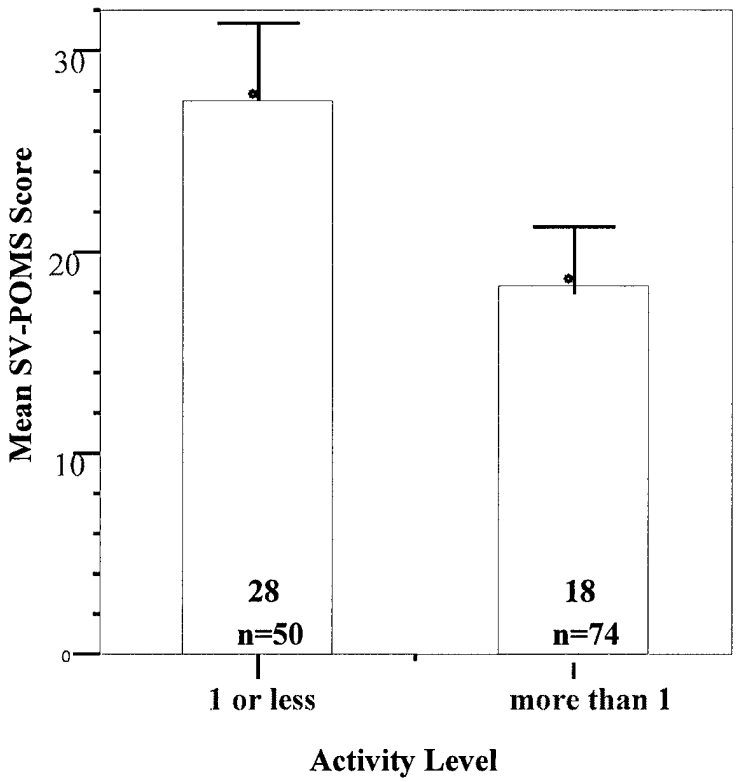


Figure 2. Predicted Values of SV-POMS by Sleep Quality

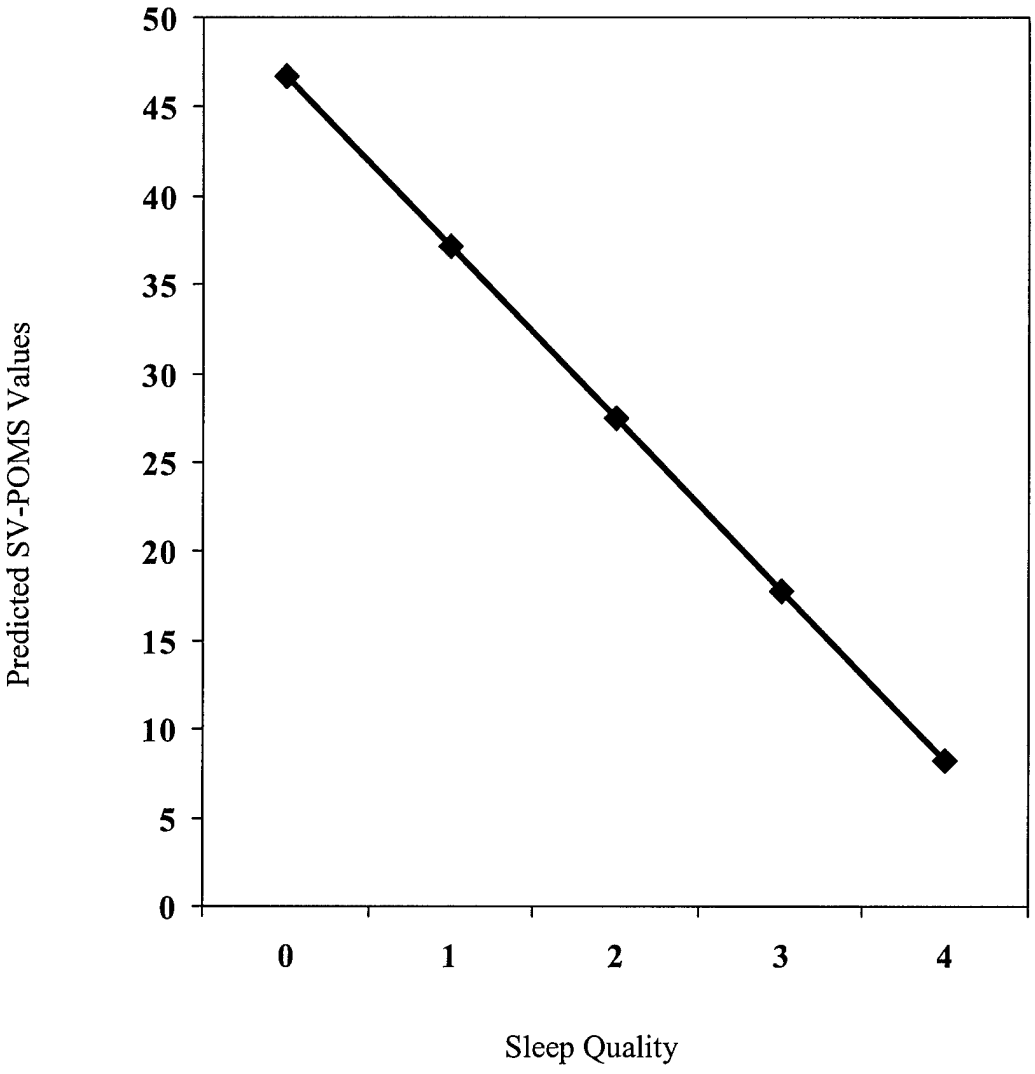
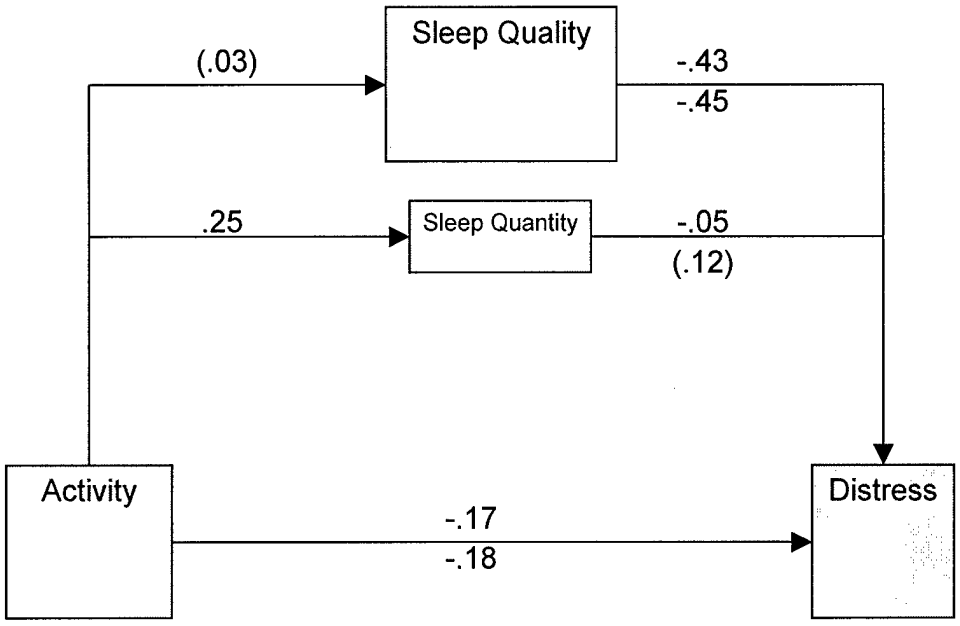


Figure 3. Correlations between Activity, Sleep and Anticipatory Distress



Note: Values above the lines represent individual bivariate regression coefficients; Values below the lines represent standardize beta coefficients with all variables entered in the regression model; Values in parentheses are non-significant ($p>.05$).

Table 1. Simultaneous regression analyses of activity, sleep quality and the interaction of activity and sleep quality as potential predictors of patient distress (SV-POMS subscales).

Predictor	B	β	p
	SV-POMS Tension		
Activity	-.78	-.06	.76
Sleep Quality	-1.93	-.36	.01
Act*Sleep Qual	-.37	-.09	.68
	SV-POMS Depression		
Activity	-5.18	-.39	.06
Sleep Quality	-2.79	-.50	.01
Act*Sleep Qual	1.32	.31	.17
	SV-POMS Hostility		
Activity	-3.80	-.32	.12
Sleep Quality	-2.25	-.45	.01
Act*Sleep Qual	.89	.24	.30
	SV-POMS Vigor		
Activity	.88	.07	.74
Sleep Quality	-.14	-.03	.84
Act*Sleep Qual	-.42	-.11	.65
	SV-POMS Fatigue		
Activity	-5.00	-.45	.02
Sleep Quality	-2.49	-.53	.01
Act*Sleep Qual	1.17	.33	.13
	SV-POMS Confusion		
Activity	-4.54	-.52	.01
Sleep Quality	-2.18	-.59	.01
Act*Sleep Qual	1.31	.47	.04

Note: df = (1,120) in all cases.

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Environmental risk factors for breast cancer among African-American women†

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Keywords

environmental • breast cancer • African-American • environment-gene • occupational • risk • susceptibility • vulnerability • gene-environment

Abstract

There are few unequivocably established environmental carcinogens for breast cancer in women. Nevertheless, environmental factors are believed to explain much of the international variation in breast cancer risk and possibly differences among racial/ethnic groups. Along with lifestyle, some adverse exposures may be higher in minority racial/ethnic groups and in underserved populations that experience higher ambient contamination. Associations have been found between environmental agents and breast cancer in subgroups of women who can be identified by common susceptibility traits as well as by timing of exposures at certain milestones of reproductive life. Susceptibility can be defined by social, environmental, and genetic modalities-factors that may predominate in certain racial/ethnic groups but that also transcend racial/ethnic boundaries. For example, genes involved in transcription and estrogen metabolism have rapid variants that are more prevalent among African-Americans, yet risk accompanying metabolic changes from these genes will prevail in all racial/ethnic groups. Lack of reliable exposure assessment remains a principal obstacle to elucidating the role of environmental exposures in breast cancer. Resources must be identified and consolidated that will enable scientists to improve exposure assessment and to assemble studies of sufficient size to address questions regarding exposure, susceptibility, and vulnerability factors in breast cancer. Breast cancer studies should be expanded to examine combinations of chemicals as well as competing or complementary exposures such as endogenous hormones, dietary intake, and behavioral factors. Cancer 2003;97(1 Suppl):289-310. © 2003 American Cancer Society.

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Article Text

Other than radiation and alcohol, few environmental exposures to our knowledge have been associated clearly with breast cancer etiology in any racial/ethnic group. Nevertheless, environmental etiologies have been invoked to explain the failure of known risk factors to account entirely for the occurrence of breast cancer. Based on studies of twins and of families with cancer in Sweden, recent estimates indicate that > 60% of breast cancer risk has an environmental component.[1][2] Environmental factors, including diet, also are believed to account for some of the disparity in breast cancer rates noted among racial/ethnic groups. African-American and white women in the U.S. are reported to have similar overall rates of breast cancer. However, compared with white women, African-American women have a higher incidence of breast cancer before age 40 years, and their prognosis after a diagnosis of breast cancer is reported to be poorer across all ages.[3] Differences in breast cancer incidence among racial/ethnic groups within in the U.S., along with wide international variability, suggest that environmental factors contribute to the etiology of the disease. Among African-American women within the U.S., breast cancer mortality also appears to vary geographically.[4]

Furthermore, it has been suggested that disparate exposures in conjunction with different genetic susceptibility may make African-Americans more vulnerable than white individuals to the insults of exogenous carcinogens.[4] Therefore, the investigation of environmental exposures that may have a differential impact on breast cancer etiology in African-American women should be considered, and studies should seek to identify risk factors that might reduce or even eliminate these disparities in incidence and mortality. Of particular urgency is the failure to understand the higher incidence of breast cancer reported among young African-American women, which may be attributable to risk factors other than established reproductive endpoints.[5]

The biologic basis for the investigation of breast cancer and environment is broad (Table 1). First, as mutagens or tumor promoters, environmental chemicals may influence carcinogenesis at many junctures in its pathway; they also may modulate the metabolic processes that activate and detoxify these pathways. In addition, environmental contaminants, acting as hormone mimics, may affect breast development and cell differentiation in early life. Therefore, to qualify as a mammary carcinogen, an environmental exposure should have the potential to operate within this proposed scheme. Environmental factors may be relevant to particular characteristics of breast cancer occurring in African-Americans: early onset, poor prognosis, and early life events such as a younger age at menarche. This temporal framework of reproductive events is described elsewhere in this supplement to *Cancer*.

Table 1. Mechanistic Framework for the Action of Environmental Agents in Breast Cancer

Gene-regulated process with potential for environmental modulation	Step in carcinogenesis	Examples of putative environmental exposure	Possible temporal window
Mammary cell development and differentiation	Susceptibility to premalignant changes	Chemicals in utero	Perinatal
Oxidation, cell turnover	Formation of procarcinogen	Modulation of gene expression	Peripubertal
		PAH epoxide, viral damage	
Detoxification	Gene mutation (DNA adduct)	PAH epoxide, free radicals	Lifetime
		Modulation of gene expression	
DNA repair	Clonal expansion, oncogene mutation	*P53* mutations by PAH	Lifetime
Growth, tumor promotion	Tumor growth, tumor recurrence	DDT, phorbol esters, DES?	Young adult
		Modulation of hormone metabolism	
Tumor progression	Tumor agressivity, metastasis	Dieldrin?	Middle age
	Metastasis		

PAH: polycyclic aromatic hydrocarbons; DDT: bis (4-chlorophenyl)-1,1,1 trichloroethane; DES: diethylstilbestrol.

Members of the Conference Workshop on Environmental Issues and Breast Cancer in African-American Women argued that although subgroups at increased breast cancer risk may be more readily identifiable in racial/ethnic groups, such entities are just as likely to exist across race and ethnicity. Examples include women with a high body mass index (BMI), variants in *BRCA1/BRCA2*, and low socioeconomic status (SES). Race/ethnicity does not imply that individuals are "genetically homogenous"; thus it is necessary to consider criteria other than just skin color to classify "at-risk" susceptible subgroups. For instance "blacks" of various ancestry (i.e., African and Caribbean) residing within the U.S. are genetically heterogenous and therefore for some scientific hypotheses it would be methodologically inappropriate to consider these groups together.

Environmental Exposures That May Be Relevant for Breast Cancer Etiology and Progression

Based on laboratory studies, a number of potential breast cancer carcinogens have been identified that also are known environmental contaminants (Table 2). More than 30 mammary carcinogens in animals and at least twice that many human carcinogens have been characterized to date.[6-8] Many of these chemicals are more likely to be encountered in an industrial environment than in settings that most women experience daily. With the advent of the so-called "endocrine disruptor" phenomenon,[9] hormonally active environmental chemicals have been targeted as potential risk factors for reproductive toxicity, including breast cancer. In a recent survey, 86 potential mammary toxins were identified and measured in household dust and air, including 9 known mammary carcinogens and 77 hormonally active agents or closely related compounds. Of these, > 30% were detected at least once in a pilot study of 3 homes (7 samples).[10] A study of occupational exposure to these compounds found approximately 30% of women to have hormonally active exposures in their workplace.[11]

Table 2. Known Mammary Carcinogens in Rodents

Benzene, butadiene	Mutagenic agents
3-MC, DMBA, aromatic amines	
EDB, VC, CCl_4, CH_2Cl_2	
MNU and analogs	Hormonal agents
DES, E2	

3-MC: 3-methylcholanthrene; DMBA: dimethylbenzanthracene; EDB: ethylene dibromide; VC: vinyl chloride; CCl_4: carbon tetrachloride; CH_2Cl_2: dichloromethane; MNU: methylnitrosourea; DES: diethylstilbestrol; E2: estradiol.
Adapted from: Huff J. Breast cancer risks from environmental chemicals. *Eur J Oncol.* 2000;5:127-132; Dunnick JK, Elwell MR, Huff J, Barrett JC. Chemically induced mammary gland cancer in the National Toxicology Program's carcinogenesis bioassay. *Carcinogenesis.* 1995;16:173-179; and Wolff MS, Weston A. Breast cancer risk and environmental exposures. *Environ Health Perspect.* 1997;105(Suppl 4):891-896.

The carcinogenic polycyclic aromatic hydrocarbons (PAH; e.g., 3-methylcholanthrene and dimethylbenzanthracene [DMBA]) and heterocyclic amines (HAA) are ubiquitous in the environment and arise from many ambient and food sources. In addition, a large variety of compounds currently in commerce (e.g., styrene, chlorinated alkanes and alkenes, and pesticides) are analogs of the chemicals listed in Table 2; relatively few have been tested for carcinogenic potential. Other chemicals (bis(4-chlorophenyl)-1,1,1trichloroethane [DDT], polychlorinated biphenyls [PCBs], and atrazine) that are not acknowledged breast carcinogens are known to enhance or inhibit tumor growth.[12][13] The organochlorines (OCs), including DDT, PCB, 2,3,7,8-tetrachlorodibenzodioxin (TCDD), polybrominated biphenyls (PBB), and phenoxy acids as well as solvents, may reduce cell-mediated immune function.[14] A number of environmental agents have been investigated in epidemiologic studies with respect to their potential influence on breast cancer risk. However, few of these have been examined in terms of their specific relation to breast cancer risk in African-American women. The quality of the exposure assessments in studies conducted to date varies greatly, and few or no data are available regarding exposures to the majority of these chemicals. Therefore, obtaining better exposure information is perhaps the most challenging part of environmental cancer research.

Occupational exposures to chemicals usually are higher than those in other surroundings, providing the opportunity to determine cancer risk among workers, either by identifying work-related exposures within specific cancer types or by enumerating cancer occurrence within jobs that have known chemical or physical contamination. Studies have investigated

the incidence or mortality of all cancer types in specific occupations, and some results support an environmental etiology for breast cancer in both African-American and white women workers. However, there are limitations to such studies (see Goldberg et al.[15] for a discussion of these issues). Of primary concern in many of the studies are the imprecise or poorly classified exposures or disease status, the examination of breast cancer mortality rather than incidence, and the lack of information regarding confounders. Furthermore, occupational cohorts often have too few women diagnosed with breast cancer, whereas case-control studies often have too few women within a given occupational group available for analyses. Either situation reduces statistical power to examine hypotheses. Poor assessment of exposure or disease is likely to result in attenuated risk estimates, whereas failure to consider confounders can overestimate or underestimate study findings. Finally, conclusions drawn from mortality studies of breast cancer often can be misleading with regard to understanding etiology because approximately 67% of women who survive the disease are excluded. However, such research often points the way to more carefully designed analytical studies.

In occupational research, evidence that chemical exposures may increase the risk for breast cancer incidence or mortality is most consistent among school teachers and managerial personnel.[16-18] However, it is not obvious that these jobs would have high carcinogenic exposures, and it is possible that other risk factors such as reproductive history were not assessed adequately.[19][20] Among the multiethnic occupational studies is a large-scale retrospective analysis that included approximately 4000 breast cancer deaths among African-Americans; both African-American and white women were found to have a higher risk of mortality from breast cancer if they had experienced higher levels of various metal exposures.[21] In addition, solvents and styrene posed an increased breast cancer mortality risk in this study. Among women who had worked in chemical, pharmaceutical, printing, or electrical equipment manufacturing industries in New Jersey, the risk of death from breast cancer among African-American women, but not white women, was elevated.[22] A recent study of hairdressers and barbers, who are exposed to a variety of genotoxic and mutagenic chemicals, included 19,980 deaths among white women and 3602 deaths among African-American women.[23] Slight elevations in the risk of breast cancer mortality were found (mortality odds ratio [OR] of 1.10 [95% confidence interval (95% CI), 1.03-1.17] for whites and a mortality OR of 1.15 [95% CI, 0.98-1.36] for African-Americans). Other occupational studies, although not including minority women, have supported the association between an elevated breast cancer risk and potentially carcinogenic chemical exposures in the workplace. These reports include exposures to PAH and benzene exposures,[24] to solvents and pesticides,[16] among dry-cleaning, auto repair, gas station workers,[25] and textile and apparel jobs.[26]

Female farmers generally have a lower risk of breast cancer compared with nonfarmers, possibly because of protective reproductive factors such as a late age at menarche or vigorous physical activity.[18][27] For example, in a recent population-based case-control study, female farmers exhibited an overall lower risk of breast cancer than women who did not work on a farm. However, in this population, female farmers exposed to pesticides were at greater risk of developing breast cancer.[28] This study, the Carolina Breast Cancer Study (CBCS), is the only study published to date that has reported extensively on environmental risk factors for breast cancer incidence among a sizeable number of African-American women. Enrollment recently was completed for the study, which includes > 800 cases and a similar number of population-based controls; currently published articles include approximately 600 African-Americans (300 cases and > 300 controls; R.C. Millikan, personal communication). Another potential population will be derived from a large-scale prospective follow-up study of 64,000 African-American women that is still underway. A major goal is to assess risk factors for breast cancer, of which incident cases are identified every 2 years through follow-up questionnaires. Limited information regarding environmental exposures will be available.[29]

Individual Environmental Agents, Suspected to Be Mammary Carcinogens, and Reported Risks in African-American Women

Ionizing radiation is the most well established environmental risk factor for breast cancer. Based on information from groups with very high exposure, it is known that nearly all the excess risk occurs among women who were exposed during adolescence and who are diagnosed with breast cancer at a relatively early age.[30][31] In a study of survivors of childhood cancer, 68% of whom received radiation therapy, breast cancer was found to be the most common of all second malignancies regardless of gender.[32] It also had the longest latency of all second tumors (a median of 16 years after diagnosis of the first cancer). The CBCS found a modest, nonsignificant risk among women exposed to ionizing radiation between ages 10-19 years (OR of 1.6; 95% CI, 0.4-7.8); these data were adjusted for race, but separate analyses were not conducted for African-Americans.[33] The majority of studies of workers exposed to low levels of radiation (e.g., weapons facilities), generally over an extended time period, reportedly have not observed an increased breast cancer risk even in the higher ranges of such exposure.[15] Admittedly, the failure to detect associations may be attributable to methodologic limitations in these studies.[15] Pilots and flight attendants have been studied for cancer risk related to excess high-altitude radiation exposure. There were suggestive increases of breast cancer among flight attendants,[34][35] but it has been noted that other factors such as parity may account for these findings.[36]

Another environmental exposure that has been examined frequently in relation to breast cancer is electromagnetic fields (EMF). In several studies of male breast cancer, an elevated risk was observed among men employed in either electrical,[37][38] telephone,[39] or railroad[40] occupations that have been linked with higher EMF exposure. Some studies of female workers also support an association between EMF and breast cancer risk,[41-43] yet the majority do not appear to (as reviewed by Caplan et al.[44]). Furthermore, the inconsistent results of studies examining other sources of EMF exposure such as residential proximity to power lines[45-52] or electric blanket use[52-57] do not appear to corroborate a

harmful relation between EMF and breast cancer risk. Thus, to date, the reported findings have not shown a consistent link between EMF and breast cancer risk. However, as a recent comprehensive review concluded, the verdict is still not in given that methodologic limitations may explain the variation in findings from these studies.[44]

Cigarette smoking is not an acknowledged breast cancer risk factor, but there has been sustained interest in its evaluation because chemicals in cigarette smoke are potent mammary carcinogens in rodents and are human carcinogens for other organs (e.g., lung, bladder, and lymphatic system).[58] The majority of studies examining smoking alone as a breast cancer risk factor do not support an overall association,[58-61] including two studies examining this association in African-American women.[5][62] Failure to detect an association may be due to the fact that tobacco smoke has been hypothesized to have dual influences on breast cancer risk. It may increase risk by either acting directly as a genotoxic agent or by acting as a promoter, but may reduce risk through its antiestrogenic properties.[60][63] These contradictory influences on risk may be dependent on the age of the individual or the time period of exposure to tobacco smoke.[64] Nevertheless, both would be of relevance to breast cancer etiology among African-American women. Genotoxic exposures derived from tobacco use are most likely to be carcinogenic to the breast during early life; this finding would apply mainly to activity of chemical components as primary carcinogens, as with ionizing radiation. Animal and in vitro studies strongly support this idea (i.e., that mammary cells at an early stage of development are more susceptible to PAH-induced tumorigenesis).[65-67] Epidemiologic studies that have investigated the question have found some hints of elevated breast cancer risk among women who report smoking as teenagers,[33][58] as well as among women exposed to passive smoke at younger ages[64] or who actively smoked during their first pregnancy.[68]

At later stages of tumorigenesis, smoking may exert an effect by acting as a promoter or by causing mutations in genes related to tumor suppression and progression (Table 1). Postmenopausal women in the CBCS exhibited higher risk if they had been smokers in the past (OR of 1.5; 95% CI, 1.0-2.4) or in the recent past (OR of 3.4; 95% CI, 1.4-8.1, adjusted for race and age).[69] In the interim between tumor initiation and progression to malignancy, cigarette smoke may exert its antiestrogenic effects, thereby reducing a woman's risk of breast cancer.[64] Thus, ignoring the timing of exposure may obscure the underlying relation between tobacco smoke and breast cancer risk. Likewise, Morabia et al. observed a positive association between tobacco smoke exposure and breast cancer when the reference group was restricted to women that not only had never actively smoked but who also had never been exposed to passive smoke,[70] suggesting that previous studies may have failed to detect an association as a result of unrecognized exposures within their referent group.[71-73] Genetic modulation of tobacco smoke exposures is considered below.

PAH and HAA compounds are among the putative carcinogens in cigarette smoke, and they also are present in foods cooked at a high temperature, smoked foods, charcoal-broiled meats, and air pollution. HAA exposures may be derived predominantly from cooked meat. A number of recent studies have examined relations between the intake of cooked meat and breast cancer risk; some[74][75] but not all[76][77] studies reported significant associations.

PAH themselves are prototypical mammary carcinogens in rodents,[78] but links between PAH exposures and breast cancer, and indeed with other malignancies, in humans are not definitive. As with smoking, the possible mechanisms are complex; PAH and their metabolites can be agonists or antagonists in hormonal pathways, making the epidemiologic characterization of risk even more difficult.[60][79] PAH exposure can be estimated via questionnaire or biologic measures. Questionnaire assessment of exposure relies on recall of experiences that occurred in the distant past. Unlike HAA, PAHs are found in many pollution sources, making accurate exposure assessment complicated. Conversely, the ability to measure the genotoxic agent (PAH-DNA adducts) in target tissue presents an excellent opportunity for more precise, objective exposure assessment. However, the lifetime of such adducts is relatively short, requiring the assumption either that the current measure of exposure is indicative of the individual's exposure at the time of carcinogenesis or that exposures are related to late-stage advancement of tumor development. Alternatively, it has been argued that higher levels of such adducts in an individual serve as a biomarker of greater susceptibility.[80]

Two separate studies, not conducted among African-Americans, found no relation between PAH-DNA adducts in breast tissue and a history of smoking, food intake, or P53 expression.[81][82] Such findings suggest a lack of specificity between these sources of exposure and the biomarker of exposure. Two studies that included African-Americans quantified PAH-DNA or aromatic-DNA adducts in breast tissue, but no significant differences in adduct levels were reported based on race/ethnicity.[82][83] Nor were case-control differences between PAH-DNA adducts in breast tissue found to be significant when adjusted for race, although there was a positive association with breast cancer risk.[83] One of these investigations found more adducts in breast adipose than epithelial cells, which may have a bearing on the presumed mechanism of action (i.e., paracrine action [across cell types] vs. autocrine function [direct changes within the cell]).[82]

PAH-related mutations have been identified in the tumor suppressor gene *P53*, which may inactivate the gene's tumor suppressor function and augur for poor prognosis. One of these mutations has been reported to be more common among African-Americans than whites and to have greater geographic variability,[84][85] suggesting an environmental origin.[4] However, in the largest study of P53 expression in tumors among African-Americans published to date, no differences among three ethnic groups, including whites and Hispanics, were found.[86]

In addition to assessment issues, repair systems for PAH damage in biologic systems are efficient, and thus the associations between PAH-DNA adducts and cancer may be very weak or may be limited to small subgroups of

susceptible individuals.

OCs are neutral, persistent, lipid-soluble agents that have been widely used as pesticides or electrical insulating fluids. They have the potential to enhance or inhibit hormonal actions. As such, they may influence tumor development or growth.[12][13][87-89] Because OCs are not complete carcinogens, any significant increases in risk conferred by OC exposure may require the presence of other risk factors. Interactions between hormonally related risk factors (reproductive history, BMI, and progression) and OCs as reported in several studies[90-92] could be explained as late-stage promoting activity by these compounds, the type of activity they exhibit in biologic models.[12][14] Similarly, modulation of cytochrome P450 enzymes (or their *CYP* genes) by OCs leads to alterations in hormone metabolism and to oxidative damage that may contribute to tumor development throughout its timecourse.

Studies over the past 30 years consistently have found OC compounds to be present at higher levels in African-Americans compared with whites,[93-95] and this pattern appears to continue. Levels of bis(4-chlorophenyl)-1,1-dichloroethene (DDE) in African-Americans are reported to be approximately twice as high as those found in whites, with somewhat similar trends reported for PCBs (Table 3).[91][96-98] Hispanic women also were found to have higher levels of OCs compared with whites in some reports. In various studies, levels of OCs in white women have reportedly declined approximately 10-fold since 1970, but this finding was not apparent in African-American women. The 10-fold decline is consistent with approximately three half-lives of elimination accompanied by no further exposure; therefore, African-Americans may continue to be exposed and they also may have longer clearance times that are attributable to both metabolic capacity and a higher BMI. Therefore, if there is a threshold dose for breast cancer risk with OCs, then the low levels currently reported among white women may fall below that, whereas risk may yet be discernible in African-American women.

Table 3. Comparison of Organochlorine Levels in African-Americans versus Whites

	African-American			White				
	DDE	PCB	No.	DDE	PCB	No.	Basis	Reference
FL, 1960s[a]	13	-	70	8.2	-	64	Whole	Davies et al., 1969[93]
SC, 1968-rural[a]	11	0.3	> 100	3	2.3	> 100		Finklea et al., 1972[95]
SC, 1968-urban[a]	6	1.9	> 100	3	3.1	> 100		
CA, 1964-1971[b]	43	4.5	50	35	4.2	50	Whole	Krieger et al., 1994[97]
NC, 1993-1996[b]	1690	510	270	760	380	389	Lipid	Millikan et al., 2000[91]
NYC, 1994-1997[b]	1000	800	69	550	650	193	Lipid	Wolff et al., 2000[98]
CT, 1994-1997[b]	1930	-	< 100	917	-	< 100	Lipid	Zheng et al., 1999[96]

DDE: bis(4-chlorophenyl)-1,1 dicholoroethene; PCB: polychlorinated biphenyls.
[a] Parts per billion, means or geometric means, among noncancer subjects in recent studies.
[b] Parts per billion, means or geometric means, among control subjects in recent studies. Lipid basis is approximately 200. OR × OR whole serum in the majority of reports.

A great many reports currently exist regarding the relation between OC exposures and breast cancer risk, mainly with regard to DDE and PCBs, which have been measured in bodily fluids at the time of diagnosis or not long before. The first study to consider African-American women found a nonsignificantly elevated risk with higher DDE or PCB exposure.[97] However, DDE and PCB levels in this study were highest among African-Americans, and the association between OCs and breast cancer risk also were strongest, compared with white and Asian women, albeit in a relatively small sample size. The CBCS found that both DDE and PCBs were associated with an elevated breast cancer risk among 292 African-American cases and 270 controls (the OR for PCB was statistically significant at 1.7 with a 95% CI of 1.0-3.0). There was no apparent association between 456 white cases and 389 controls.[91] Again, in this study levels of DDE and PCBs were higher among African-American women. The majority of the case-control studies with the largest sample sizes (> 300 cases) have been comprised primarily of white women, and found no significant associations between individual OC residues measured in blood or adipose tissue and breast cancer risk in the overall population.[99-102] Similarly, a pooled analysis of 1400 cases from 5 studies, primarily white individuals, found no increased risk of breast cancer with exposure to DDE or PCB when adjusted for race.[102] Nevertheless, some studies have reported increased risks between one or more OC compounds and breast cancer onset[104-108] or poorer prognosis.[92][101]

Associations have been found between OCs and breast cancer risk within subgroups that may be related to hormonal

factors, including women who had not breastfed,[90] postmenopausal women,[109] and women with the rapid CYP1A1 genotype.[110] In the CBCS, in which both DDE and PCBs were associated with risk among African-Americans, higher levels of exposure to specific OC compounds were found to be associated with an increased breast cancer risk in certain subgroups of women, including African-American women in the upper tertile of BMI (PCB: OR of 4.9; 95%CI, 1.6-14.8) and African-American women in the lowest tertile of BMI (DDE: OR of 3.8; 95% CI, 0.98-15.1), as well as African-American and white women who were parous but had never breastfed (for both DDE and PCB).[91] Given these observations among African-American women in the CBCS, and their consistency with other studies,[90] further investigation may be warranted regarding the effect of OC exposure on breast cancer risk with respect to reproductive milestones, including pregnancy, menopause, and pubertal development.[111][112] In addition, the higher levels of OCs among African-Americans and their poorer prognosis would warrant the investigation of breast cancer incidence, recurrence, and survival with regard to hormonally active xenobiotics such as these. Finally, OCs possess a range of hormonal activity (estrogenic, antiandrogenic, antiestrogenic, etc.). Therefore, specific mechanisms may be relevant to African-American women, whose hormonal profiles have been shown in some studies to differ from white women at different times of life.[113-116]

Other Exposures

Certain solvents and related small molecules including the chloroethylenes are reported to be carcinogens in animals and some are mammary carcinogens (Table 2).[8][117] Many of these substances commonly are found in the ambient environment, in public water supplies, and around hazardous waste sites. A few ecologic studies have assessed risk for breast cancer with such exposures, although some initial associations subsequently have been suggested to be the result of confounding factors.[118] In North Carolina, halomethanes in drinking water (chlorination byproducts of water treatment) were quantified by zip code but were not found to be associated significantly with breast cancer in either African-American or white women.[119] Nitrates in water, an indicator of mutagenic exposures, were quantified on a community basis in Iowa, and associations with some malignancies were found, but not with breast cancer.[120] In another study, atrazine (a hormonally active herbicide) was quantified at the county level and was found to be associated with breast cancer risk.[121] A study of women on Long Island, New York, in which the addresses of women in a case-control study of breast cancer were linked with proximate high-traffic sites or chemical facilities having carcinogenic emissions, found a higher risk among postmenopausal women living closer to the sources of exposure.[122] In Massachusetts, case-control studies of breast cancer have investigated estrogenic chemical exposures that occurred in previous occupations and tetrachloroethylene contamination of municipal water supplies; no significant associations were found, but there were suggestions of positive associations with tetrachloroethylene.[11][123] However, these studies suffer many of the same shortcomings as occupational studies, including difficulty in adjusting for confounding factors such as reproductive history. In addition, the ecologic studies cannot quantify exposures on an individual basis, leading to imprecisely characterized risk. However, many chemicals, including solvents, are short-lived in the body and historic assessments can be the only way to estimate exposures.

Factors That Act in Concert with Exposures to Link Environment with Breast Cancer Etiology and Progression

The majority of environmental exposures today either exist at concentrations too low or have carcinogenic potential too weak to be easily identified as risk factors, in contrast with very strong associations between smoking and lung cancer or between radiation and various cancers. Therefore, modifying factors that make some women more susceptible to the effects of environmental agents must be identified to elucidate any role of the environment in breast cancer. Exposure assessments and factors that create or influence susceptibility can be examined within several contexts, an approach that may benefit research among African-American women but that would encompass susceptible women of any racial/ethnic group. Four contexts were envisioned by this Workshop as being central to the investigation of environmental agents and exposure modifiers in breast cancer.

Context 1. Environment/environment interactions

Mammary carcinogens may interact with other exposures to increase risk above and beyond the risk associated with each individual exposure. Therefore, epidemiologic research and laboratory investigations must ascertain effects of multiple as well as single exposures, thereby advancing the understanding of joint effects. Exposures interacting with one another can have a direct and/or a modifying effect on disease risk. Combinations of exposures have not been well studied because of biologic as well as epidemiologic study design complexities. A major obstacle to the study of joint exposures is the need for large numbers of participants with complete risk factor assessments.

Some information concerning the resultant effect of multiple exposures can be gleaned from laboratory studies with the OCs, in which a combination of chemicals has been administered, usually at staggered timepoints, to assess promoter or initiator potential in animal models. The timing of tumor-promoting, tumor-inhibiting, or tumor initiating exposures is critical.[124] Examples include dioxin (TCDD; an antiestrogenic chemical), DDT, and PCBs as tumor promoters and PAH or MNU as tumor initiators.[12][13][87] Many in vitro studies have found effects to be additive.[125-127]

Environment/environment interactions may occur between exposures of very different origins, such as chemicals and viruses. Solvents, DDT, TCDD, and PCBs are immunotoxic,[128] and some chemicals of this kind have been implicated as cofactors in hematopoietic malignancies that have a viral etiology,[14][129] including PCBs and non-Hodgkin lymphoma.

[130][131] Given the recently revived interest in viral etiologies for breast cancer,[132-134] investigation of cofactors such as OCs that may be secondary to viral immunosuppression could be relevant. Also, by compromising T-cell immune function, OCs and other such immunotoxic exposures may serve as late-stage promoters of cancers that originate through other mechanisms.

The examination of joint exposures should take into account endogenous hormones, which are considered carcinogens and may act as mutagens as well as transcription factors. Hormone levels can be affected by many factors including BMI, alcohol intake, and diet. Examples can be found in the study of OCs in relation to breast cancer risk. Associations between OCs and breast cancer risk in the CBCS differed according to BMI among African-American and white women.[91] BMI has been reported to have a major influence on the disposition and metabolism of persistent OCs.[135-137] Furthermore, BMI and weight gain have been reported to be associated independently with postmenopausal breast cancer risk,[138-142] possibly through the elevation of steroid hormones synthesized in peripheral adipose.[143] Weight at the time of breast cancer diagnosis[144] and weight gain after diagnosis[145][146] also have been linked to increased breast cancer mortality and recurrence. Moreover, BMI is related to reproductive development, including puberty and age at menarche, [147] which in turn have been reported to be associated with breast cancer risk.[148] Therefore, BMI may affect the bioavailability of OCs as well as hormones in women.

Clearly, research on environment and breast cancer must be incorporated into a larger picture of the complex hormonal milieu that is critical for the development of breast cancer. An individual's hormonal profile is determined by an array of factors encompassing both genetic and environmental influences. Such factors are hypothesized to account for the majority of the differences between premenopausal and postmenopausal breast cancer risk, as well as for breast cancer related to family history and early age at diagnosis; risk likely will be better explained by a combination of these factors. [149] Environmental/lifestyle risk factors can confer risk that varies among subgroups classified according to hormonal factors. For instance, a stronger protective effect for breast cancer has been reported for a higher (versus lower) intake of fruits and vegetables among 1) premenopausal compared with postmenopausal women, 2) women who consume more alcohol compared with those who consume less, and 3) among women with a family history compared with those without. [150-153] It is possible that African-American women, and especially those who are at high risk for breast cancer, possess an elevated hormonal profile that may enhance or reduce their response to certain environmental insults, derived from both exposures and from modifying genes.[154]

Context 2. Environment/gene interactions

Environment-gene interactions have the potential to alter the course of carcinogenesis at many steps along the way by mutagenesis and gene regulation. Environment-gene interactions include 1) genes that control the Phase I enzymes responsible for converting environmental exposures to mutagenic metabolites; 2) genes that control Phase II enzymes that convert metabolites of environmental toxins to inactive forms; 3) genes responsible for DNA repair; 4) oncogenes and tumor suppressor genes. Environmental exposures can also act as hormone mimics and thus as transcription factors to alter the expression of genes, or that can induce gene expression including that of Phase I enzymes.[155][156] A schematic example is shown in the Figure 1 for metabolizing genes.

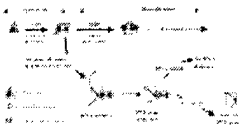

Figure 1. Schematic for damage to DNA by the electrophilic metabolite of an enzymatically oxidized environmental toxin, resulting in a *P53* mutation.
[Normal View 20K | Magnified View 66K]

Inherited genetic capacity for metabolism is believed to explain wide interindividual variations in biologic measures of dose, such that even people with comparable exposures can have quite different internal or target-organ levels. Differences in metabolic capacity may provide quite different susceptibility patterns among African-American women exposed to environmental carcinogens when compared with other racial/ethnic groups. Unlike the rare genetic variants (e.g., *BRCA1* mutations) typically associated with a high risk for cancer, the genome contains numerous more common genetic variants (present at > 1-50%), including genes that govern bodily "housekeeping" functions or that indirectly influence metabolic capacity. The idea of individual susceptibility is aptly illustrated by the example of smokers, who do not all experience lung cancer, whereas smoking accounts for much of lung cancer risk. An additional example is that of BRCA gene mutation carriers, among whom it has been estimated that 30% will never suffer from cancer.[157]

BRCA1/BRCA2 and other high-penetrance genes may have low-prevalence variant alleles that carry a very great risk for subsequent cancer, but they appear to account for little of the overall attributable risk for the disease because inherited mutations exist in altogether < 10% of the population. When a mutation in one copy of the *BRCA1/BRCA2* (or *P53* or *AT*) gene is inherited, cancer is believed to ensue only if a somatic mutation occurs in the second copy of the gene, resulting in reduced function as a tumor suppressor or in DNA repair. Because these genes are such powerful guardians of the genome, damage may result in short latency (time between exposures and clinically detectable disease) and a young age at the time of diagnosis of cancer. Thus, even high-penetrance genes that pose a greatly increased cancer risk may undergo mutations from environmental toxins; protective exposures may prevent these changes.

Studies of genetic variants in metabolizing genes, including the examples shown in Table 4, generally have reported few or

no consistent increases in breast cancer risk with the gene variant alone.[110][158] This is not surprising given that the gene variants under study are quite common and may affect risk over a long latent period by acting in concert with relevant exposures, including hormones.[159] Compared with the more straightforward and strong (monogenic) risks accompanying *BRCA1/BRCA2* mutations, carcinogenesis evolving from metabolic pathways requires cumulative, multiple steps, a process that has been termed polygenic.[159][160] Studies that have found increased risks with gene variants alone will be discussed along with the gene exposure findings.

Table 4. Examples of Genes that Modulate Environmental Agents: Prevalence (%) of Variants

			African-American	White
		Reference	Range of reported values	
Phase I metabolizing genes	*CYP1A1*, MSPI (wt/var; wt/var)	[158],[170],[180]	13-31%; 3-5.8%	21-39%; 2-5%
	CYP1A1, Ile-Val (wt/var; wt/var)	[170],[179],[180]	3.7-4.4%; 0%	9-15%; 1.1%
	CYP1A1, MSPI-AA (wt/var; wt/var)	[170],[179]	15-20%; 0-1.9%	0%; 0%
	CYP2E1 (2 sites, allele frequency)	[244]	0.02-0.09	0.02-0.08
	CYP1B1 rapid, gene frequency	[174],[175]	70-75%	35-40%
	*NAT1** 10 rapid	[245]	76%	38%
Phase II conjugation/detoxification genes	$NAT2^0$ (null; 4-7 alleles)	[245-247]	40-64%	56-74%
	$GSTM^0$ (null)	[158],[244],[245]	13-41%	52-62%
	$GSTT^0$ (null)	[158],[244],[245],[248]	17-29%	16-27%
	GSTP (val/val)	[245]	23%	11%
DNA repair gene	*XRCC1* (cod399 glnallele frequency)	[207]	0.14	0.36
Tumor suppressor, repair, etc.	*P53* 2-1-2 haplotype	[249]	37%	78%
	1-2-1 haplotype		32%	9%

wt/var: wild type/variant; val/val: valine/valine; NAT: n-acetyl transferase; GST: glutathione-*S*-transferase.
Data from breast cancer studies were from controls for whom information was available.

Susceptibility: variability in metabolizing enzymes
Phase I metabolizing enzymes.
The majority of the susceptibility genes that have been investigated with regard to environmental exposures can be implicated in cellular oxidative damage that may contribute to the carcinogenic process. Oxidized species, or reactive molecules, are created by Phase I enzyme activation of exogenous agents (Table 2), from endogenous hormones, and from other free radical sources, such as fatty acid oxidation. Many of the genes controlling this process have a higher frequency of the at-risk variant in African-Americans (Table 4). A general marker of genotoxicity is oxidative damage to

DNA (e.g., levels of 8-OHdG and 5HMDU in the blood, urine, or tissues). Biomarkers of this kind have shown a much wider variation among African-American women compared with white women.[161] A well studied research area of oxidative damage involves exposure to PAH, which can be metabolized to the genotoxic PAH diol-epoxide metabolites by cytochrome P450 (*CYP*) enzymes; higher levels of the diol-epoxide are found with the more rapid metabolizing Phase I genotype.[162] HAAs are similarly activated by N-acetyl transferase (*NAT*). Therefore, if African-American women have high adverse exposures in combination with a greater prevalence of the related adverse genotype(s) then excess risk may ensue; this might be manifest in measures of primary oxidative DNA damage (ODD), of tissue damage, or in other diseases related to similar damage. Enzymes of this kind also are involved in the uptake and delivery of pain medications, chemotherapy drugs, and hormones that may be substrates for several enzymes (e.g., CYP1A1 and CYP1A2). Such variability has been proposed to explain how tamoxifen metabolism differs among racial/ethnic groups, in a way that adversely affects the response to tamoxifen among African-Americans.[163]

Phase II metabolizing enzymes.
Phase II detoxification or deactivating enzymes conjugate genotoxic oxidation products from environmental exposures into readily eliminated metabolites including sulfates, glucuronides, and acetates. If deactivation mechanisms were lower in a subgroup with excessive oxidative damage, then this subgroup might be at an increased risk for a number of diseases. A number of examples demonstrate how Phase II enzymes alter individual levels of biomarkers of exposure. Oxidative damage measured as 8-OHdG was reported to be highest in urine from neonates whose mothers were both exposed to tobacco smoke and null glutathione-*S*-transferase (*GST*); levels were successively lower in nontobacco-exposed women with null *GST* and tobacco-exposed women with *GST*, and were lowest among those with no tobacco smoke exposure who had GST activity.[164] In addition, women with breast cancer who carried the *GST*-null genotype were found to have higher PAH-DNA adducts in tissue compared with controls,[165] a finding that parallels experiments in cell lines.[166] NAT, which can activate HAAs, can also detoxify electrophilic intermediates. To illustrate the role of NAT2 detoxification, persons with slow NAT2 phenotypes accumulated higher levels of 3-aminobiphenyl-hemoglobin adducts; among racial/ethnic groups, the average adduct levels were directly proportional to the NAT2 slow phenotype, which varied 4-fold: 14% slow (Asians; the lowest adduct levels), 34% slow (African-Americans), and 54% (whites).[167] These relations were independent of racial/ethnic status. The combination of *GSTM*-null with the NAT-slow phenotype also was found to be related directly to adduct level.[168] With the possible exception of *GSTP*, African-Americans appear to have a higher proportion of null genes for conjugating activity compared with whites (Table 4).

In epidemiologic studies, more significant findings for the gene variant alone with breast cancer risk have been reported for the Phase II deactivating enzymes compared with Phase I pathways. One explanation could be that there is a temporal advantage in their assessment at later stages of carcinogenesis, for example if oxidative damage affects late-stage tumor promotion or tumor suppression. However, there are multiple metabolic pathways that control oxidation processes. Deficiencies in DNA-repair genes plus a lower intake of dietary antioxidants also would be adverse for risks related to oxidative damage.

Genes that control metabolizing enzymes
The majority of genes related to metabolism (Table 4) are expressed primarily in the liver, so that a carcinogenic effect on mammary epithelium would require that active metabolites be transported to the breast, unless they have an indirect effect such as to raise or lower systemic hormone levels. GST and CYP1A1 are expressed in breast tissue, although the isoforms do not necessarily reflect the known gene variants.[168-170]

Phase I metabolizing genes.
Chemicals of particular interest to breast cancer, including PCBs, DDT, PAH, cigarette smoke, and HAA, can induce some of these enzymes and can be substrates for their own transformation. CYP2D6 and CYP2E1 also may be up-regulated by or may catalyze the metabolism of environmental agents, including cigarette smoke components, alcohol, and small molecules such as those shown in Table 2. The at-risk variants in both *CYP2D6* and *CYP2E1* are uncommon (< 10%, Table 4 and reference 172). Because the prevalence of the known gene variants is low, current epidemiologic studies are too small to detect a gene effect that yields a relative risk below 2.[173] Pooled analysis of epidemiologic studies indicated that relative risk from the gene variant alone would be < 1.5 for *CYP1A1*, *NAT1/2*, *CYP2D6*, *CYP2E1*, and *GSTT*.[173] Hormone synthesis and metabolism also are governed by several Phase I enzymes that can be induced or inhibited by environmental exposures.[159] In a mammary tumor model, PAH increased levels of both CYP1B1 and CYP1A1 in normal tissue but only CYP1B1 was increased in tumor tissue.[79] Thus xenobiotics may be able to alter the hormone sensitivity of tumors. CYP1B1 metabolizes estrogen (as well as PAH) and the rapid variant is more common among African-American women compared with white women.[174][175] The variant was associated with increased risk of breast cancer among Chinese women (allele frequency of 53%),[176] but not among African-American or white women in another small study.[175]

Among the Phase I enzymes, CYP1A1 is the most well studied. There are four *CYP1A1* variants that have been scrutinized in epidemiologic studies; genotoxic potential is suspected for minor variants that code for more rapid metabolism and that are inducible by various exposures. Two of the identified variants are more prevalent among whites than African-Americans. Another variant is specific to African-Americans (MSPI-AA) and has been reported to be more common in African-American women with breast cancer and to be associated with higher levels of adverse estrogen metabolites.[158][177] However, the number of patients studied was very small, and the findings have not yet been

reproduced in other populations of African-Americans. The MSPI variant is more common among Asian women and was found to be associated with higher risk of breast cancer in a study in Taiwan[178][179] whereas the wild-type genotype was found to be associated with early-onset breast cancer in whites.[180] The *CYP1A1*4* variant was found to confer a higher risk in another study, especially among postmenopausal women.[181] Other U.S. studies (mainly of white women) have found associations for breast cancer among women who smoked before age 18 years and who also had 2 *CYP1A1* variants.[182] The Ile-Val variant was associated with risk among long-time smokers[183] and among women with higher PCB exposures.[110]

Phase I/II metabolizing genes: NAT.
The *NAT* gene family can N-oxidize HAA and related compounds, rendering the rapid form as the at-risk genotype. However, the NATs also conjugate, or deactivate, oxidative intermediates; slow metabolizers would be at risk if this were the exposure of interest. Therefore, findings regarding environment-gene interactions with the N-acetyl transferases are conflicting, but this is not remarkable given the complex, multiple pathways through which these genes may act. The *NAT2* and *NAT1*10* rapid genotypes were reported to confer a higher risk for breast cancer among recent smokers in the CBCS (race-adjusted risk estimates); just as the null genotype is rarer, the rapid genotypes are more common in African-Americans than in other ethnic groups (Table 4).[69] A study of whites found a higher risk of breast cancer among smokers with the rapid *NAT1*11* genotype.[184] Two studies among white women found higher risk for smokers who also had low activity *NAT2* compared with nonsmokers.[185][186] One of these studies also found a higher risk among women smokers who had rapid *NAT2* genotypes.[186] A third study found a nonsignificantly increased risk for smokers with low-activity NAT2.[187][188]

Because the NAT enzymes activate HAA, they have been investigated in relation to reported dietary intake of cooked meat, although not specifically among African-Americans. One study has found an association between rapid *NAT2* or rapid *NAT1*11* and the intake of meat or well-done meat.[184][189] The same study found an increased risk of breast cancer with low-activity sulfotransferase alone or with two high-activity alleles and a higher meat intake.[190] Three other reports found no risk associated with *NAT2* and meat intake.[76][77][191] In a case-control study performed in Taiwan, slow acetylators were at higher risk for breast cancer, and this finding was found to be significant among postmenopausal but not premenopausal women.[192]

Another environment-gene example of Phase II metabolism that deserves further attention is the higher risk observed for breast cancer occurring among postmenopausal white women with the inactive *MnSOD* genotype, especially those with a lower intake of fruit, vegetables, and antioxidants, consistent with higher oxidative damage.[193] This association was not found in a preliminary report from the CBCS, which included African-Americans; furthermore, the frequency of low-activity *MnSOD* was reported to be similar in African-Americans and whites.[194] Protection by dietary intake of antioxidants or increased risk from oxidative exposures may have to be taken into account in addition to the reduced activity genotype for both Phase I and Phase II enzymes.

Phase II metabolizing genes: GST.
The GST family of enzymes conjugates electrophilic substances to their glucuronide metabolites, which are biologically inactive and are excreted readily. The at-risk genotype lacks GST activity; known *GST*-null genotypes are reported to be less common in African-Americans compared with whites (Table 4). *GST*-null genotypes themselves in the majority of studies reportedly have shown no or weak associations with breast cancer risk, both among African-Americans[158][195] and whites.[183][195-197] In the CBCS, *GSTM* and *GSTT* null genotypes were found to be associated with increased risk among women diagnosed at an earlier age (adjusted for race) or those with a family history.[195] Among whites, one study found null *GSTM1* to be associated significantly with breast cancer risk, whereas *GSTT* and *GSTP* null demonstrated positive but nonsignificantly increased risk.[198] Elevated risk was found for *GSTP1* null, but not for GSTM1-null, among women with a family history.[199] There also was an increased risk for *GSTM1*-null among older patients in two studies [200][201] and a slightly lower risk of early-onset breast cancer in two studies.[180][197] However, a pooled analysis indicated that alone, *GSTM1* and *GSTP* null variants confer a modest (less than twofold) increased risk of breast cancer. [173] Thus in vulnerable subgroups *GST*-null may pose a risk for breast cancer, perhaps in conjunction with the age at onset of cancer or with a family history among women with relevant exposures.

Of particular interest for African-Americans, who are reported to have a poorer prognosis after a diagnosis of breast cancer, *GSTM* and *GSTT* null genotypes were reported to be related to longer survival in a study of 240 cases of white women,[202] although not in a smaller study.[203] Moreover, the null variant may be protective against disease recurrence by improving response to chemotherapies that result in oxidative damage.[204] Because of the lower frequency of null *GSTM1* among African-Americans, more rapid progression of breast cancer in this population potentially may be related to these genes. Conversely, studies of GST expression in tissue have been reported to find no correlation with survival.[170] [171] Nevertheless, these associations are consistent with a possible effect of GST on reducing oxidative damage or opposing other hormonally related oxidative pathways throughout life. In addition, early onset, family history, and poor survival are risk patterns that are significant for African-American women, but these profiles also may be common to a risk subgroup that responds poorly to oxidative damage; such a group may be able to be characterized in part by null *GST*, along with other dysfunctional deactivating enzyme profiles, regardless of ethnicity.

DNA repair.

Genetic susceptibility to breast cancer after radiation exposure as well as other genotoxic exposures may be related to rare gene variants including germline mutations in *BRCA1/BRCA2* and the *AT* gene.[205][206] Studies of these highly penetrant genes among African-Americans are discussed elsewhere in this supplement. Because the variants in these genes are so rare, research is limited with regard to their interactions with environmental factors. In contrast, a common variant exists in the *XRCC1* base excision repair gene, which was reported to be associated with increased breast cancer risk among African-American women who had the rare allele (codon 399 gln)[207] Among African-Americans, breast cancer risk also was found to be elevated for women with the homozygous *XRCC1* wild-type gene who had a history of smoking, whereas among white women the wild-type gene was found to be associated with breast cancer only among those women with a past exposure to ionizing radiation. The *XRCC1* wild-type gene was associated with a higher prevalence of deletions in the *P53* gene in breast tumors among African-American women with radiation exposure and more *P53* transversions among women who smoked. A number of mutations in the *P53* gene have been attributed to environmental exposures,[208] and these findings suggest a series of mutations that can arise from environment-gene processes.

Oncogenes and tumor suppressor genes

P53 is overexpressed in approximately 40% of breast tumors, with approximately 20% having mutations in the gene; these rates are similar among African-Americans, Hispanics, and whites.[86][98][209][210] P53 has many functions in development, DNA repair, apoptosis, cell cycle regulation, and transcription and as a tumor suppressor.[208] Environmental genotoxins have been linked to specific mutations, or hotspots, along the *P53* gene, with some being characteristic of environmental mutagens such as PAH. The resulting P53 mutational spectrum appears to vary with ethnicity and geographic distribution, which is consistent with an environmental etiology.[4][210] Furthermore, as many as 10 inherited variants have been found in the *P53* gene; these differ by race/ethnicity and possibly are associated with a risk of breast cancer.[173][210-212] Potential evidence of an environmental influence on P53 inactivation includes the observation that P53 overexpression in tumors is associated with a history of smoking, which is consistent with a genotoxic effect of smoking on *P53*.[209] In addition, evidence from the CBCS suggested different *P53* alterations were found with smoking versus radiation exposures.[207]

The rare HRAS alleles are associated with breast cancer, an association that may be stronger in African-Americans.[213] Moreover, some polymorphisms in the *HRAS* gene are more common among African-Americans than whites.[212] Environmental exposures have been implicated in *HRAS* mutations.[212][214] A significant positive association between *HRAS* mutations and breast cancer risk also was observed in a pooled analysis of nine studies.[212]

Transcriptionally active genes

Estrogen receptor (ER)-negative breast tumors are implicated in the poor prognosis of breast cancer occurring among African-American women.[4] Limited but inconclusive evidence suggests that gene variants in the *ER* are associated with the risk of breast cancer,[171] although studies of these variants have not been reported among African-Americans. There are at least two ERs (ER-α and ER-β) that potentially are highly relevant to environmental exposures and are expressed in different tissues.[215][216] Hormones and environmental agents have different affinities for ER-α and ER-β. The action of many compounds, including the OCs as transcription factors, is believed to be mediated through the ER or other hormone receptors (e.g. the androgen receptor).[217]

Another transcriptionally active gene (*UGTA1A*) appears to have a more potent variant among African-Americans; in the CBCS, an elevated risk of breast cancer was found among premenopausal African-American women who possessed this variant, with a suggestion of a higher risk among those women with ER-negative breast cancer.[218]

In addition, levels of hormone synthesizing and metabolizing enzymes may be induced by environmental substances and thereby alter levels of other exposures. One example is the up-regulation of P450 enzymes by drugs, dioxin, or broccoli, shifting the ratio of estrogen metabolites in favor of 2-hydroxyestrone over 16α-hydroxyestrone.[156][219]

Summary of environment-gene interactions

Individual genes and their targeted substrates have been studied with regard to breast cancer risk, but few studies published to date have included African-American women. Nevertheless, the majority of genetic variants exist in all populations, albeit in different proportions. Therefore, the average metabolic profile of racial/ethnic subgroups may be shifted to the degree that variant alleles predominate. Regardless of race, a combined effect of environmental exposures, metabolizing genes, and hormone synthesis and metabolism on breast cancer risk is suggested by evidence from both experimental and epidemiologic research; compared with other racial/ethnic groups, African-Americans appear to have different distributions of a number of the genes controlling these processes, in particular *NAT2*- and *CYP1B1*-rapid alleles. The phenotypic potential, or the overall distribution of such genotypes, appears to hold great promise for identifying an environment gene or profile associated with breast cancer risk. Future research also should attempt to incorporate a pharmacokinetic-based compartmental approach to exposure assessment that would incorporate pharmacogenetics (i.e., dose time-gene models) and provide an integrated (time-relevant) dose picture over a woman's lifetime. Dietary intake also is important to consider with metabolizing enzymes, particularly antioxidants, which, with detoxifying enzymes, may reduce oxidative damage and thereby alter both the transcriptional and mutagenic effects of environmental agents.

Concept 3. Environment/social interactions

Environmental epidemiologic research generally has disregarded the fact that environmental exposures are entwined intimately with social, behavioral, and psychosocial factors. Statistical models usually include SES and race/ethnicity, but SES is measured rather crudely (e.g., by annual income or educational level). Research has suggested that SES accounts for much of the racial/ethnic variability in breast cancer incidence or mortality.[220] Both factors should be considered to obtain a more complete picture of breast cancer risk in the U.S.[221] Other investigators believe that geographic differences in breast cancer mortality can be explained by reproductive factors and lifestyle variations across various regions in the U.S.[113][222] Furthermore, it has been proposed that two socially influenced factors play an important role in breast cancer risk: tissue susceptibility brought on by reproductive factors such as early menarche and higher exposures to carcinogens.[223]

The concept of environmental justice has emphasized the idea that higher exposures to carcinogens often exist in underserved populations and that these populations also contain a disproportionate number of minority groups, including African-Americans.[224] An environmental justice approach would suggest that SES and reproductive factors may be responsible for the higher levels of OCs reported in African-Americans and Hispanics.[214] Type of housing, its upkeep, and geographic location can dictate the type, number, and level of exposure. In addition, stress can arise from poverty and other inadequacies with regard to quality-of-life issues, and these may render such individuals more vulnerable to the adverse effects of exogenous exposures.[225] For example, stress may compromise immune function through a psychophysiological mechanism or secondary to infectious diseases that arise from psychosocial stress or indigence.[226][227] This, in turn, may increase the risk for breast cancer from environmental exposures that lower immune response. It has been theorized that the type of tumor may represent socioenvironmental exposure.[154] Therefore, the environment-social context into which environmental exposures are incorporated can describe a biobehavioral environmental model for breast cancer risk, and this context would include socially vulnerable subgroups regardless of racial/ethnic status.[225]

Context 4. Temporal effects, or timing of environmental risk factors

The biologic sequence of events leading to cancer no doubt coincides with certain times of vulnerability during life and latency for cancer (Table 1). Much epidemiologic and experimental evidence suggests the need to investigate mutagenic exposures that occur early in a woman's life, even in utero.[228] Studies of breast cancer suggest that the intrauterine environment, age at menarche, and age at first birth as well as the interval between these latter two events may be critical periods in the development of breast cancer.[229][230] For example, being a twin or being heavier at birth appears to increase breast cancer risk whereas maternal preeclampsia or breastfeeding has been reported to decrease the risk in the daughter.[230] To reiterate examples given earlier in this article, ionizing radiation and cigarette smoke are purported to exert a primary carcinogenic effect relatively early in life, whereas immunotoxic or tumor-promoting activity may support later stages of tumorigenesis.

Russo et al. have argued that the peripubertal and early postpartum periods are highly likely periods for tumor initiation to occur.[65][124] It also has been suggested that exposures after menarche but prior to first pregnancy are more detrimental because the breast cells are undergoing differentiation and proliferation during this interval and therefore are more vulnerable to carcinogenic exposure.[231] Experimental research has established that tumor initiation is most effective during early breast development.[65][124][214][232] In vitro studies further suggest that mammary epithelial cells from virgin rats produce more mutagenic PAH metabolites than do cells from pregnant rats.[67] In addition, in laboratory studies, perinatal exposures can alter ductal and lobular development within the breast.[233] However, little research in humans has been performed in this area.

Age at puberty is approximately 1 year earlier among African-Americans,[234] and age at menarche has been consistently younger compared with that of whites during this century by approximately 6 months.[113][234] This finding potentially has great impact for cancer risk, because early menarche may explain, in part, the higher rates of premenopausal breast cancer among African-American women compared with white women in the U.S.[113][235] As suggested earlier, a younger age at puberty and menarche could provide a longer period of vulnerability to insult by environmental carcinogens on the breast tissue. Studies have identified some environmental exposures that influence age at puberty and/or menarche as well as other factors believed to be associated with reproductive function (such as cyclicity and fecundity). In animals, a large number of chemical exposures may alter the onset of puberty (vaginal opening).[236][237] In support of this experimental data, Gladen et al.[112] reported a positive association among girls with in utero exposures to PCBs and weight gain during puberty, although no association was found with pubertal stage. White girls exposed to higher versus lower levels of PBBs in utero reportedly experienced an earlier age at menarche.[111] To our knowledge, no comparable data exist for nonwhite children. Chemical exposures also have been reported to be associated with menstrual function during the reproductive years.[238] In addition, cyclicity and age at menopause have been linked to stress as well as smoking and this finding has been observed in African-American women.[239] Rogan et al. observed a shortened duration of lactation among women with the highest exposures to DDE.[240][241] Because a long duration of lactation may be protective for later breast cancer, these findings offer an additional mechanism by which environmental exposures may alter a woman's risk for breast cancer many years before breast cancer diagnosis.

We believe more research is needed to identify environmental exposures experienced in early life that may affect breast cancer risk.[4] These exposures may affect tumorigenesis only indirectly, making risk ascertainment very difficult. Therefore, research efforts should be directed toward determining how environmental exposures may alter known risk

factors, including timing of puberty/menarche, menstrual function, fecundity, lactation, and age at menopause. As reviewed elsewhere in the current supplement, early life and other reproductive factors among African-American women, as well as among other racial/ethnic groups, confer a risk for breast cancer (generally less than twofold). Because breast cancer risk may vary depending on the timing of exposure, the future examination of environmental risk factors should take into consideration the age or time period in a woman's life during which these exposures occur.

RESOURCES ARE NEEDED TO BE ABLE TO LINK ENVIRONMENT WITH BREAST CANCER ETIOLOGY AND PROGRESSION EFFECTIVELY

Efforts must be made to identify resources for undertaking research concerning the role of environment in the development of breast cancer, both with regard to populations available for study and methodologies used to assess multiple risk factors. Opportunities should be developed that will enable research to be undertaken within the contexts of the environmental etiologies discussed earlier. A number of general as well as specific opportunities were suggested by the Environmental Working Group.

Large populations can be combined to enhance existing studies. Future studies must include African-American women or must identify susceptible or vulnerable subgroups. Attempts to pool existing and future data, biologic samples, or other population resources should be made to elucidate risks that affect African-American women. Newly funded studies should collaborate in the early stages of the research so that data collected can be combined effectively in later analyses.

Studies should be undertaken among highly exposed or uniquely exposed women, including those working in occupations and industries with intense exposures to carcinogens or hormonally active agents; migrant groups so that research can elucidate the role of migration and acculturation; uniquely exposed groups such as migrant farm workers (pesticides) and populations living on or near environmental justice/superfund sites; and in the case of male breast cancer to determine risk factors among blacks.[242]

Focus groups may help to identify new exposures and appropriate contexts for the assessment of risk.

Groups of women with early-onset breast cancer would enable researchers to assess differing risk factors in such women, but it also would be possible to then examine risk in sisters, mothers, and daughters (and sons!) of the affected women.

Registries of affected persons exist already for special studies; environmental assessment could be added on to existing studies of African-American women (at least five or six such efforts were identified by the Workshop).

Research should be encouraged that will develop better tools for exposure assessment and for ecologic, occupational, cohort, and case-control studies.

In keeping with the theme that etiologic and prognostic factors are useful only in so far as they are generalizable, newly identified population resources must preserve the ability to study individual populations while enabling the results to be linked with other research. Efforts must continue to implement existing recommendations that are particular to breast cancer that develops in African-American women. Examples include recent reports from the Institute of Medicine on Cancer in Minorities and on Gender Differences in Susceptibility to Environmental Factors.[243]

Conclusions

Evidence suggests that environmental factors and genetic susceptibility are associated with breast cancer risk, although there is a paucity of research among African-Americans. Compared with white women, African-American women as well as women of other racial/ethnic minorities may have higher levels of exposures to certain environmental agents that have been implicated in increasing the risk of breast cancer. They also may have greater genetic susceptibility to the biologic effects of such exposures. When possible, future studies should include women of all racial/ethnic backgrounds to elucidate environment-gene as well as social factors in breast cancer etiology. In addition, research should consider how genetic, social, and environmental factors act within the complex hormonal milieu that leads to the development of breast cancer.

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Occupation and breast cancer in women 20–44 years of age (United States)

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Abstract

Objective: To examine the relation between breast cancer risk and job history among women 20–44 years of age who participated in a multi-center, population-based, case–control study.
Methods: Participants consisted of women newly diagnosed with breast cancer (1642) and controls identified by random-digit dialing (1494). Details about the three longest jobs were collected and coded by an industrial hygienist. Odds ratios and 95% confidence intervals were calculated and adjusted for age, study site, and other breast cancer risk factors.
Results: Several occupational and industrial categories were found to influence breast cancer risk. Stratification of the study population by parity revealed differences in breast cancer risk between the two groups for several occupational categories, including *teachers, librarians or counselors* (increased risk only among parous women) and *natural scientists and mathematicians* (decreased risk only among nulliparous women).
Conclusions: This is among the first population-based case–control studies to examine occupational history and breast cancer risk in young women, with the ability to consider a wide array of potential confounders, including reproductive characteristics. This study provides further evidence of an increased breast cancer risk for several occupations and industries. Other findings were not as strongly supported by previous investigations.

Introduction

Migration studies suggest that a woman's environmental exposures may influence her risk of breast cancer [1]. Such exposures may include those received while at work. In 2001, women comprised 47% of the employed US workforce, and almost three quarters of women between the ages of 20 and 45 were employed [2], making it important to consider occupational exposures as potential breast cancer risk factors.

Occupational exposures have been studied less thoroughly than other potential risk factors for breast cancer, so examination of occupation in relation to breast cancer risk provides an opportunity to identify potential sources of exposures not regularly considered or investigated. The workplace can expose women to chemical, biological, or physical agents that could influence breast cancer risk. Women who work in manufacturing, chemical and pharmaceutical industries may be exposed to chemical solvents [3]. Health care professionals, including physicians and nurses, may be exposed to chemotherapeutic agents, various chemicals,

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and ionizing radiation [4]. Electromagnetic field (EMF) exposure has been examined as a possible risk factor, and women with occupations in the electrical and electronics industries as well as occupations requiring extensive use of computers may be exposed to EMF [5]. Further, jobs that require higher levels of physical activity have been proposed to decrease breast cancer risk [6, 7].

Currently, there is no strong evidence that any particular occupation influences breast cancer risk [8]. Occupations that have been adversely linked to breast cancer risk include teachers, chemists, health care workers, as well as professional and technical occupations, although the evidence is inconsistent [3]. The elevated risk among women employed in these occupations has often been attributed to reproductive characteristics such as delayed childbirth, reduced number of children or little or no breastfeeding. However, several of these professions (*e.g.*, chemists and health care professionals), as well as others (*e.g.*, cosmetologists), may involve exposure to chemicals that are potential breast carcinogens [4]. Relatively few comprehensive studies of job history and breast cancer have been conducted. Using detailed information on the three longest held occupations and their corresponding industries, which can indicate potential occupational exposures, this relation was examined among young women who participated in a multi-center, population-based, breast cancer case–control study.

Materials and methods

The methods of this study have been described previously [9]. The main objectives of the Women's Interview Study of Health were to investigate the relation of breast cancer in women under the age of 45 with oral contraceptive use, alcohol consumption, diet, and other characteristics. In brief, study participants were identified in three geographic regions (Atlanta, GA; Seattle, WA; and central NJ) between May 1, 1990 and December 31, 1992. Cases were 20–44 newly diagnosed with breast cancer. Controls, identified through random-digit dialing (RDD) [10], were women who had never been diagnosed with breast cancer, frequency matched to the anticipated age distribution of cases by five-year age group and study site.

Structured in-person interviews were completed by 1642 cases (84.4%) and 1496 controls (78.2%). The overall control response rate (product of RDD screener and interview response rates) was 70.8%. Subject refusal was the main reason women did not complete the interview (6.6% for cases and 12.9% for controls); physician refusal accounted for 5.8% of case non-participation. This study was approved by the institutional review board at each of the participating institutions and signed informed consent was obtained from all study participants. The interview included questions on demographic factors, reproductive and menstrual history, contraceptive behavior, use of exogenous hormones, medical history, body size and physical activity, diet, alcohol consumption, smoking, and family history of cancer. The relation between many of these factors and breast cancer risk has already been examined. Oral contraceptive users and alcohol drinkers as well as women who had a late age at first birth, an early age at menarche, an induced abortion, a previous breast biopsy, a first degree relative with breast cancer, or a low BMI were found to be at increased breast cancer risk [9, 11–16]. However, waist to hip ratio, cigarette smoking, miscarriages, electric blanket use, and recreational exercise were not found to be positively associated with breast cancer risk [9, 12, 17–19].

During the interview, an occupational history of the three jobs held for the longest time was obtained; all reported jobs had to have been held for six months or longer. Details collected on each job included the position title, usual activities or duties performed, what the company made or did, the start year, and the total number of years of employment. Using this information, a trained industrial hygienist assigned industry and occupation codes according to the 1987 Standard Industrial Code (SIC) [20] and 1980 Standard Occupational Code (SOC) [21]. The detailed SIC and SOC codes were then grouped according to their overriding classifications. Twenty-four women reported that they were never employed for at least six months and none of the participants reported having been a housewife as any of their three longest held jobs. Two control women refused to provide information about their occupational history leaving 1494 controls and 1642 cases for inclusion in the analyses.

Duration of work in a particular occupation or industry was categorized as never, less than five years, or five + years. Latency, the number of years that elapsed between starting work in an occupation or industry and the reference date (the date of diagnosis for cases, and the date of RDD telephone screening for controls) was categorized as never, less than 10 years, or 10+ years.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using unconditional logistic regression [22]. To estimate the associated breast cancer risk for each occupation, we considered women who had never held that job as unexposed. Similarly, to estimate the risk associated with working in a particular industry, we considered women who had never worked in that

industry as unexposed. All logistic regression models were adjusted for the frequency matching variables (age and geographic site). The following covariates were considered as potential confounders: menopausal status; age at menarche; age at first birth; number of live births; ever breast fed; level of education; marital status; race; body mass index (BMI, weight in kilograms/height in meters squared); ever use of oral contraceptives; smoking history; usual alcohol use; average lifetime weekly recreational physical activity; history of breast biopsy; and family history of breast cancer. Of these factors, age at first birth, number of live births, and level of education were retained since their inclusion resulted in the most parsimoniously adjusted model relative to the age- and geographic site adjusted models. To avoid unstable and uninformative estimates of association, ORs were only calculated for an individual job or industry category if at least 10 cases and 10 controls reported working in the category. Tests for trend in duration and latency were conducted if successive levels were increasing or decreasing. Presence of a trend was determined by examining the statistical significance of a categorical variable with the values of 0,1,2 indicating the level of duration (never, <5 years, 5+ years) or latency (never, <10 years, 10+ years).

Results

The number of jobs reported by each woman ($\chi^2 = 3.2$, $p = 0.4$) and employment duration (14.1 *versus* 13.6 years, $p = 0.05$) did not differ by case–control status. However, parous case women started working before having their first child more often than parous controls (75.7 *versus* 70.2%, $\chi^2 = 9.3$, $p < 0.01$). Similar proportions of cases and controls reported having held only one job (19.7 and 21.6%) while less than one percent of each group reported never having been employed for at least six months. The most frequently held occupations among cases and controls, respectively were: *service* (24.8 and 29.2%); *marketing and sales* (23.6 and 22.3%); *executive, administrative and managerial* (20.5 and 20.1%); *teachers, librarians and counselors* (17.6 and 14.5%); and *secretaries, stenographers and typists* (17.3 and 15.4%). Industries commonly worked in by cases and controls, respectively were: *finance, insurance and real estate* (21.6 and 20.0%); *services industry: educational services* (21.2 and 20.1%); *services industry: health services* (20.0 and 22.0%); and *retail industry: eating and drinking places* (11.3 and 12.8%).

The estimates of association for the majority of occupations examined were not substantially different from one (Table 1). Two occupational categories, *handlers, equipment cleaners, helpers and laborers* and *computer and peripheral equipment operators*, were suggestive of an increased risk with ORs greater than 1.5; however as evidenced by the wide CI, the estimates were unstable. The occupation group, *teacher, librarian or counselor* had a weaker, but positive association with borderline significance (OR = 1.3, 95% CI: 1.0, 1.6). Several occupations were suggestive of decreased risk with unstable estimates of effect of less than or equal to 0.7. Among these occupations with the strongest inverse association, only the estimate for *writers, artists, entertainers or athletes* approached statistical significance (OR = 0.7, 95% CI: 0.5, 1.0).

For women who were or *adjusters, investigators or collectors* increased breast cancer risk was only associated with having worked in this occupation for less than five years or having started 10 or more years prior to reference date. *Teachers, librarians or counselors* who worked for shorter, but not longer, periods of employment were at significantly increased risk (OR = 1.6, 95% CI: 1.2, 2.2); breast cancer risk did differ when examined by latency. Both *production work* and *material recording, scheduling, and distributing clerks* were suggestive of an increased breast cancer risk for women employed in these occupations for longer, but not shorter durations. Employment in the latter category was also suggestive of an increased risk if work started 10 or more years prior to reference date. A similar latency pattern was observed for the *social scientist, social worker, religious worker, or lawyer* category. The suggested decreased breast cancer risk for *writers, artists, entertainers and athletes* became more pronounced for women who only held these jobs less than five years (OR = 0.4, 95% CI: 0.2, 0.8). A difference in breast cancer risk according to latency was observed for *health technologists and technicians* with increased risk associated with starting work closer to but not farther from reference date.

Stratification of the study population by parity revealed differences in breast cancer risk between the two groups for several occupational categories (Table 2). Nulliparous women who were *natural scientists and mathematicians* were at decreased risk (OR = 0.4, 95% CI: 0.2, 0.9) while parous women employed in this category were not. Increased risk was suggested among nulliparous, but not parous, women who worked in the occupational categories: *social scientists, social workers, religious workers and lawyers*; *record clerks*; and *miscellaneous administrative support.* Parous, but not nulliparous, women who were *teachers, librarians and counselors* or *adjusters, investigators and collectors* were at increased risk of breast cancer (OR = 1.3, 95% CI: 1.0, 1.7 and OR = 1.5, 95% CI: 0.9, 2.5, respectively).

Table 1. Adjusted ORs and 95% CIs for breast cancer in relation to ever having worked in a specific occupation among women under age 45 in Atlanta, New Jersey and Seattle, 1990–1992

Occupation[a]	Ever held job ≥6 months								Duration				Latency (years started job before reference date)			
									<5 years		5+ years		<10 years		10+ years	
	Ca	Co	OR[b]	95% CI	OR[c]	95% CI	OR[d]	95% CI	OR[c]	95% CI	OR[c]	95% CI	OR[c]	95% CI	OR[d]	95% CI
Executive, administrative and managerial	342	302	**1.0**	0.9 1.2	**1.0**	0.8 1.2	**0.9**	0.8 1.1	**1.0**	0.7 1.3	**1.0**	0.8 1.2	**1.1**	0.9 1.5	**0.9**	0.7 1.1
Natural scientists and mathematicians	43	46	**0.8**	0.5 1.3	**0.7**	0.5 1.1	**0.7**	0.4 1.0	–	– –	–	– –	**0.6**	0.3 1.2	**0.8**	0.5 1.4
Social scientists, social workers, religious workers and lawyers	92	63	**1.4**	1.0 1.9	**1.3**	0.9 1.8	**1.2**	0.9 1.8	**1.2**	0.7 2.1	**1.3**	0.9 2.0	**1.0**	0.6 1.8	**1.5**	0.9 2.3
Teachers, librarians and counselors	294	218	**1.2**	1.0 1.5	**1.2**	1.0 1.6	**1.3**	1.0 1.6	**1.6**	1.2 2.2	**1.1**	0.8 1.4	**1.2**	0.8 1.7	**1.3**	1.0 1.6
Registered nurses, pharmacists, dieticians, therapists and physician's assistants	107	90	**1.1**	0.8 1.4	**1.1**	0.8 1.4	**1.1**	0.8 1.5	**1.1**	0.6 2.1	**1.0**	0.7 1.4	**0.9**	0.5 1.7	**1.1**	0.8 1.5
Writers, artists, entertainers and athletes	76	86	**0.8**	0.6 1.1	**0.7**	0.5 1.0	**0.7**	0.5 1.0	**0.4**	0.2 0.8	**0.9**	0.6 1.4	**0.6**	0.4 1.1	**0.8**	0.5 1.1
Health technologists and technicians	62	69	**0.8**	0.6 1.2	**0.8**	0.6 1.2	**0.9**	0.6 1.3	**1.0**	0.5 1.9	**0.8**	0.5 1.2	**1.5**	0.8 3.1	**0.7**	0.5 1.0
Technologists and technicians, except health	81	82	**0.9**	0.7 1.2	**0.9**	0.6 1.2	**0.9**	0.6 1.2	**0.9**	0.6 1.3	**0.8**	0.5 1.3	**0.7**	0.5 1.2	**0.9**	0.6 1.4
marketing and sales	394	336	**1.1**	0.9 1.3	**1.1**	0.9 1.3	**1.1**	0.9 1.3	**1.2**	1.0 1.5	**1.0**	0.8 1.3	**1.1**	0.8 1.4	**1.1**	0.9 1.4
Administrative support occupations, including clerical																
Supervisors	96	102	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.6**	0.4 1.0	**1.0**	0.7 1.4	**0.6**	0.4 1.0	**1.0**	0.7 1.4
Computer and peripheral equipment operators	22	11	**1.8**	0.9 3.7	**1.9**	0.9 3.9	**1.8**	0.8 3.8	–	– –	–	– –			–	– –
Secretaries, stenographers and typists	289	232	**1.1**	0.9 1.4	**1.1**	0.9 1.4	**1.1**	0.9 1.4	**1.2**	0.9 1.6	**1.1**	0.9 1.4	**1.0**	0.6 1.5	**1.2**	1.0 1.4
General office	140	137	**0.9**	0.7 1.2	**0.9**	0.7 1.2	**0.9**	0.7 1.2	**0.9**	0.6 1.2	**1.0**	0.7 1.4	**1.1**	0.7 1.7	**0.9**	0.7 1.2
Information clerks	72	81	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.7**	0.5 1.1	**0.8**	0.5 1.2	**0.8**	0.5 1.4	**0.5**	0.3 1.0	**0.9**	0.6 1.4
Correspondence clerks and order clerks	28	24	**1.0**	0.6 1.8	**1.0**	0.6 1.8	**1.0**	0.6 1.7	**1.1**	0.5 2.2	**0.9**	0.4 2.2	–	– –	–	– –
Record clerks	69	52	**1.2**	0.8 1.7	**1.2**	0.8 1.7	**1.2**	0.8 1.8	**1.2**	0.8 1.8	**1.2**	0.6 2.5	**1.3**	0.6 2.4	**1.1**	0.7 1.8
Financial record processing	135	147	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.8**	0.6 1.1	**0.8**	0.6 1.2	**1.0**	0.6 1.6	**0.8**	0.6 1.0
Communications equipment operators	27	18	**1.4**	0.7 2.5	**1.4**	0.7 2.5	**1.3**	0.7 2.5	–	– –	–	– –	–	– –	–	– –
Mail and message distributing	13	10	**1.1**	0.5 2.6	**1.1**	0.5 2.6	**1.3**	0.6 3.2	–	– –	–	– –	–	– –	–	– –
Material, recording, scheduling, and distributing clerks	53	51	**1.0**	0.7 1.4	**1.0**	0.7 1.4	**1.0**	0.7 1.5	**0.8**	0.5 1.3	**1.3**	0.7 2.5	**0.7**	0.4 1.3	**1.2**	0.7 2.1
Adjusters, investigators and collectors	62	41	**1.4**	0.9 2.1	**1.4**	0.9 2.0	**1.5**	1.0 2.3	**1.7**	1.0 3.0	**1.0**	0.6 1.8	**1.0**	0.5 2.1	**1.6**	0.9 2.6
Miscellaneous administrative support, including clerical	149	121	**1.1**	0.9 1.5	**1.2**	0.9 1.5	**1.1**	0.8 1.4	**1.2**	0.9 1.8	**1.1**	0.8 1.6	**1.2**	0.8 1.8	**1.2**	0.9 1.6
Service	413	439	**0.8**	0.7 1.0	**0.9**	0.8 1.1	**0.9**	0.8 1.1	**1.0**	0.8 1.3	**0.8**	0.6 1.0	**0.9**	0.6 1.2	**0.9**	0.8 1.1
Agriculture, forestry and fishing	18	25	**0.7**	0.4 1.3	**0.7**	0.4 1.3	**0.8**	0.4 1.5	–	– –	–	– –	–	– –	–	– –
Mechanics and repairers	14	11	**1.1**	0.5 2.5	**1.2**	0.5 2.6	**1.2**	0.5 2.7	–	– –	–	– –	–	– –	–	– –
Precision production	39	47	**0.7**	0.5 1.2	**0.8**	0.5 1.2	**0.8**	0.5 1.3	**0.6**	0.4 1.1	**1.1**	0.5 2.1	**0.7**	0.3 1.6	**0.8**	0.5 1.4
Production working	94	97	**0.9**	0.6 1.2	**0.9**	0.7 1.3	**1.0**	0.7 1.4	**0.7**	0.5 1.1	**1.3**	0.8 2.1	**0.8**	0.4 1.5	**1.0**	0.7 1.4
Transportation and material moving	27	25	**1.0**	0.6 1.7	**1.1**	0.6 1.9	**1.2**	0.6 2.1	–	– –	–	– –	**1.0**	0.4 2.1	**1.3**	0.6 2.7
Handlers, equipment cleaners, helpers and laborers	34	22	**1.4**	0.8 2.4	**1.6**	0.9 2.7	**1.6**	0.9 2.8	–	– –	–	– –	–	– –	–	– –
No jobs held for at least 6 months	14	10	**1.1**	0.5 2.4	**1.4**	0.6 3.0	**1.6**	0.7 3.8	–	– –	–	– –	–	– –	–	– –

[a] Reference group for each occupation is composed of women who never held that specific occupation; ORs were only calculated if at least 10 cases and 10 controls reported working in the category within each stratum.

[b] Adjusted for age and geographic site.

[c] Adjusted for age; geographic site; age at first birth; number of live births; and level of education.

[d] Adjusted for age; geographic site; menopausal status; age at menarche; age at first birth; number of live births; ever breast fed; level of education; marital status; race; BMI (weight in kilograms/height in meters squared); ever use of.

Table 2. Adjusted ORs and 95% CIs for breast cancer in relation to ever having worked in a specific occupation according to parity among women under age 45 in Atlanta, New Jersey and Seattle, 1990–1992

Occupation[a]	Nulliparous only				Parous only			
	Ca	Co	OR[b]	95% CI	Ca	Co	OR[c]	95% CI
Executive, administrative and managerial	122	101	**1.0**	0.7 1.4	219	201	**1.0**	0.8 1.2
Natural scientists and mathematicians	13	23	**0.4**	0.2 0.9	30	23	**1.0**	0.6 1.8
Social scientists, social workers, religious workers and lawyers	33	17	**1.7**	0.9 3.1	59	46	**1.1**	0.8 1.7
Teachers, librarians and counselors	66	54	**1.0**	0.6 1.5	228	164	**1.3**	1.0 1.7
Registered nurses, pharmacists, dieticians, therapists and physician's assistants	29	22	**1.1**	0.6 2.0	78	68	**1.0**	0.7 1.4
Writers, artists, entertainers and athletes	26	32	**0.7**	0.4 1.1	50	54	**0.7**	0.5 1.1
Health technologists and technicians	16	12	**1.1**	0.5 2.4	46	57	**0.8**	0.5 1.1
Technologists and technicians, except health	29	25	**0.9**	0.5 1.6	52	57	**0.8**	0.5 1.2
Marketing and sales	101	77	**1.2**	0.8 1.6	293	259	**1.1**	0.9 1.3
Administrative support occupations, including clerical								
Supervisors	30	24	**1.1**	0.6 1.9	66	78	**0.8**	0.5 1.1
Secretaries, stenographers and typists	65	51	**1.0**	0.7 1.5	224	181	**1.2**	0.9 1.5
General office	32	27	**0.9**	0.5 1.6	107	110	**0.9**	0.7 1.2
Information clerks	18	16	**1.0**	0.5 2.0	54	65	**0.8**	0.5 1.1
Record clerks	18	11	**1.4**	0.6 3.1	51	41	**1.1**	0.8 1.8
Financial record processing	34	32	**0.9**	0.5 1.5	101	115	**0.8**	0.6 1.1
Material, recording, scheduling, and distributing clerks	10	10	**0.8**	0.3 2.1	43	41	**1.0**	0.7 1.6
Adjusters, investigators and collectors	18	14	**1.0**	0.5 2.1	44	27	**1.5**	0.9 2.5
Miscellaneous administrative support, including clerical	35	20	**1.5**	0.8 2.6	114	101	**1.1**	0.8 1.5
Service	87	71	**1.1**	0.7 1.6	326	368	**0.9**	0.7 1.0
Precision production	2	6	–	– –	37	41	**0.9**	0.6 1.4
Production working	14	13	**0.8**	0.4 1.7	80	84	**1.0**	0.7 1.4

[a] Reference group for each occupation is composed of women who never held that specific occupation; ORs were only calculated if at least 10 cases and 10 controls reported working in the category within each stratum.

[b] Adjusted for age; geographic site; and level of education.

[c] Adjusted for age; geographic site; age at first birth; number of live births; and level of education.

For ever having worked in a specific industry, 40 of the 49 categories (82%) had risk estimates from 0.7 to 1.4 (Table 3). Of those with an increased risk (*amusement and recreation services*; *miscellaneous manufacturing industries*; *general merchandise stores*; *justice, public order and safety*; *national security and international affairs*; and *electric, gas and sanitary services*) all categories except *miscellaneous manufacturing industries* had significant or borderline significant breast cancer risk estimates. An OR less than 0.7 was observed for women who ever worked in the following industries: *local and interurban passenger transit* (OR = 0.5, 95% CI: 0.3, 1.1); *private households* (OR = 0.6, 95% CI: 0.4, 0.9); and *rubber and miscellaneous plastic products* (OR = 0.6, 95% CI: 0.3, 1.4).

Several industries were associated with increased breast cancer risk when examined by duration and latency. The increased risk seen for having ever worked in *general merchandise stores* was more pronounced in those who did this work for less than five years (OR = 1.7, 95% CI: 1.2, 2.5) than in those who did this work for five or more years (OR = 1.3, 95% CI: 0.9, 2.0). Longer latency for working in this retail industry was associated with an increased risk of breast cancer. Having worked in the *amusement and recreation services* followed a similar pattern of association with respect to duration and latency.

Discussion

In this investigation of job history and breast cancer risk among young women, several occupational and industrial categories were identified as influencing risk. The available detailed job history allowed us to investigate breast cancer risk associated with employment duration and latency, while information on reproductive history allowed us to examine job-related risk among parous and nulliparous women. Occupations that influence breast cancer risk have been identified through epidemiologic studies of different designs using either breast cancer mortality or incidence as the outcome. We restrict our discussion to investigations of incident breast cancer, because the results of mortality studies may not be directly comparable to our results. Furthermore, mortality may be influenced by etiologic determinants as well as factors that influence survival, and mortality studies generally lack the information needed to control for the effects of potential confounding (which make interpretation of those studies' results even more difficult and less comparable).

The relationship between occupation and breast cancer has been thoroughly reviewed [3, 23]. Many of the occupations and industries for which we observed some associations with breast cancer risk have been reported on in other studies, but because of different coding methodology used among studies, occupational groups are not always identically defined. Our *adjusters, investigators and collectors* category includes a wide range of occupations, for example insurance adjusters, bill and account collectors, and customer complaint clerks [21]. Similar to our findings, one population-based registry study found a significant excess incidence of breast cancer among insurance raters and claims adjusters [24], whereas in other case–control studies no increased risk was observed for accounting/auditing clerks [25] or for insurance, bank and other finance clerks [26]. No association between working in general merchandise stores and breast cancer risk was found in a large Canadian case–control study [26], which is in contrast to our finding of increased risk. Our observation of decreased breast cancer risk associated with the occupational category of *writers, artists, entertainers and athletes* was consistent with the findings of two large studies, one conducted in the Nordic countries and the other in Canada [26, 27] but in opposition to others [24, 25, 28]. Our finding of a small increased risk for religious workers, especially among those who started in this occupation 10 or more years before reference date is supported by findings in the Nordic countries [24, 27], but not in the US [29]. The observed increased risk found among Nordic technical/chemical/physical/biological workers [27] was in contrast to our finding of decreased risk for technicians. As reported here and in two other studies, ever having been a *natural scientist or mathematician* was suggestive of decreased or no risk [25, 26].

Our finding of decreased breast cancer risk for women who had agricultural occupations is well supported in the literature [23]. One study provided some support for our finding of decreased breast cancer risk for women who worked in *private households* [26], while another did not [25]. Occupational physical activity has been proposed to lower breast cancer risk [6] which may be an underlying factor for the decreased risk observed for working in private households and agricultural jobs [7]. It is difficult to speculate on the biological plausibility of many of the other relationships because the specific exposures linking the occupation to breast cancer risk are not known. Also, it is possible that these are spurious findings given the large number of comparisons made in many occupational analyses.

As in our study, several epidemiologic studies have identified teachers [24–26, 28, 30–32] and librarians [24, 26, 29, 31] as occupational groups at higher risk of breast cancer, yet in other investigations, teachers were

Table 3. Adjusted ORs and 95% CIs for breast cancer in relation to ever having worked in a specific industry among women under age 45 in Atlanta, New Jersey and Seattle, 1990–1992

Industry[a]	Ever held job ≥6 months					Duration										Latency (years started job before reference date)									
						<5 years					5+ years					<10 years					10+ years				
	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI
Agriculture, forestry and fishing	24	33	**0.7**	0.4	1.2	13	16	**0.8**	0.4	1.6	11	17	**0.6**	0.3	1.3	17	11	–	–	–	7	22	–	–	–
Construction	43	38	**1.1**	0.7	1.7	21	15	**1.4**	0.7	2.7	22	23	**0.9**	0.5	1.6	18	15	**1.2**	0.6	2.5	25	23	**1.0**	0.5	1.7
Manufacturing																									
Food and kindred products	34	28	**1.1**	0.7	1.9	21	12	**1.7**	0.8	3.5	13	16	**0.7**	0.3	1.5	7	11	–	–	–	27	17	–	–	–
Textile mill products	11	13	**0.7**	0.3	1.7	5	7	–	–	–	6	6	–	–	–	0	2	–	–	–	11	11	–	–	–
Apparel and other textile products	28	23	**1.2**	0.7	2.1	14	14	–	–	–	14	9	–	–	–	11	4	–	–	–	17	19	–	–	–
Printing and publishing	49	45	**0.9**	0.6	1.4	24	25	**0.9**	0.5	1.5	25	20	**1.0**	0.6	1.9	16	14	**1.0**	0.5	2.0	33	31	**0.9**	0.6	1.5
Chemicals and allied products	44	50	**0.7**	0.5	1.1	16	22	**0.7**	0.4	1.3	28	28	**0.8**	0.5	1.4	11	8	–	–	–	33	42	–	–	–
Rubber and miscellaneous plastics products	11	16	**0.6**	0.3	1.4	7	9	–	–	–	4	7	–	–	–	3	3	–	–	–	8	13	–	–	–
Fabricated metal products	15	19	**0.7**	0.4	1.4	11	9	–	–	–	4	10	–	–	–	4	6	–	–	–	11	13	–	–	–
Industrial machinery and equipment	35	36	**0.8**	0.5	1.3	17	24	**0.6**	0.3	1.2	18	12	**1.2**	0.6	2.4	11	7	–	–	–	24	29	–	–	–
Electronic and other electric equipment	40	50	**0.7**	0.5	1.1	21	25	**0.8**	0.4	1.4	19	25	**0.7**	0.4	1.2	10	10	**1.0**	0.4	2.3	30	40	**0.6**	0.4	1.1
Transportation equipment	47	49	**0.9**	0.6	1.4	23	23	**1.0**	0.5	1.7	24	26	**0.8**	0.5	1.5	10	15	**0.7**	0.3	1.5	37	34	**1.0**	0.6	1.6
Instruments and related products	30	30	**0.9**	0.5	1.5	11	10	**1.1**	0.5	2.6	19	20	**0.8**	0.4	1.5	8	14	–	–	–	22	16	–	–	–
Miscellaneous manufacturing industries	18	12	**1.5**	0.7	3.2	9	10	–	–	–	9	2	–	–	–	8	6	–	–	–	10	6	–	–	–
Transportation and public utilities																									
Local and interurban passenger transit	13	24	**0.5**	0.3	1.1	5	9	–	–	–	8	15	–	–	–	8	8	–	–	–	5	16	–	–	–
Trucking and warehousing	17	12	**1.4**	0.7	2.9	12	7	–	–	–	5	5	–	–	–	5	8	–	–	–	12	4	–	–	–
Transportation by air	35	35	**0.8**	0.5	1.4	10	16	**0.6**	0.3	1.3	25	19	**1.1**	0.6	2.0	4	5	–	–	–	31	30	–	–	–
Transportation services	23	25	**0.8**	0.4	1.4	10	10	**0.9**	0.4	2.1	13	15	**0.7**	0.3	1.5	12	9	–	–	–	11	16	–	–	–
Communications	105	88	**1.0**	0.8	1.4	33	28	**1.1**	0.7	1.8	72	60	**1.0**	0.7	1.4	26	23	**1.1**	0.6	2.0	79	65	**1.0**	0.7	1.4
Electric, Gas and sanitary services	25	12	**1.8**	0.9	3.6	8	7	–	–	–	17	5	–	–	–	3	5	–	–	–	22	7	–	–	–
Wholesale trade																									
Durable goods	50	55	**0.8**	0.6	1.3	23	24	**0.9**	0.5	1.7	27	31	**0.8**	0.5	1.3	18	24	**0.7**	0.4	1.4	32	31	**0.9**	0.6	1.5
Nondurable goods	48	43	**1.0**	0.6	1.5	25	19	**1.2**	0.6	2.1	23	24	**0.8**	0.5	1.5	17	12	**1.3**	0.6	2.8	31	31	**0.8**	0.5	1.4
Retail trade																									
General merchandise stores	139	86	**1.5**	1.2	2.0	86	47	**1.7**	1.2	2.5	53	39	**1.3**	0.9	2.0	27	20	**1.4**	0.8	2.6	112	66	**1.6**	1.1	2.2
Food stores	55	59	**0.9**	0.6	1.4	36	39	**1.0**	0.6	1.6	19	20	**0.9**	0.5	1.7	14	23	**0.7**	**0.3**	1.3	41	36	**1.1**	0.7	1.8
Automotive dealers and service stations	18	14	**1.2**	0.6	2.5	8	8	–	–	–	10	6	–	–	–	5	9	–	–	–	13	5	–	–	–

Table 3. (Continued)

Industry[a]	Ever held job ≥6 months					Duration										Latency (years started job before reference date)									
						<5 years					5+ years					<10 years					10+ years				
	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI	Ca	Co	OR[b]	95%	CI
Apparel and accessory stores	57	55	**1.0**	0.7	1.4	34	35	**0.9**	0.6	1.5	23	20	**1.0**	0.6	1.9	13	11	**1.2**	0.5	2.7	44	44	**0.9**	0.6	1.4
Furniture and home furnishings stores	15	19	**0.7**	0.4	1.4	8	9	–	–	–	7	10	–	–	–	6	3	–	–	–	9	16	–	–	–
Eating and drinking places	189	193	**1.0**	0.8	1.2	118	108	**1.1**	0.8	1.5	71	85	**0.8**	0.6	1.1	39	52	**0.8**	0.5	1.2	150	141	**1.0**	0.8	1.3
Miscellaneous retail	89	82	**1.0**	0.7	1.4	54	55	**1.0**	0.6	1.4	35	27	**1.1**	0.7	1.9	37	26	**1.4**	0.8	2.3	52	56	**0.8**	0.6	1.2
Finance, insurance and real estate	361	301	**1.1**	0.9	1.3	149	119	**1.2**	0.9	1.5	212	182	**1.0**	0.8	1.3	91	96	**0.9**	0.7	1.3	270	205	**1.2**	1.0	1.4
Services																									
Hotels and other lodging places	30	39	**0.7**	0.4	1.2	17	19	**0.8**	0.4	1.6	13	20	**0.6**	0.3	1.2	9	13	–	–	–	21	26	–	–	–
Personal services	60	71	**0.8**	0.6	1.2	28	29	**0.9**	0.6	1.6	32	42	**0.7**	0.5	1.2	21	27	**0.8**	0.4	1.3	39	44	**0.9**	0.6	1.3
Business services	139	130	**0.9**	0.7	1.2	74	67	**1.0**	0.7	1.4	65	63	**0.9**	0.6	1.3	62	65	**0.9**	0.6	1.3	77	65	**1.0**	0.7	1.4
Amusement and recreation services	58	38	**1.5**	1.0	2.2	38	18	**2.1**	1.2	3.7	20	20	**0.9**	0.5	1.7	11	14	**0.8**	0.4	1.7	47	24	**1.8**	1.1	3.0
Health services	334	331	**0.9**	0.8	1.1	102	120	**0.8**	0.6	1.1	232	211	**1.0**	0.8	1.2	71	79	**0.9**	0.6	1.2	263	252	**0.9**	0.8	1.1
Legal services	58	43	**1.2**	0.8	1.8	17	18	**0.9**	0.4	1.7	41	25	**1.4**	0.9	2.4	14	16	**0.8**	0.4	1.8	44	27	**1.4**	0.9	2.3
Educational services	354	303	**1.0**	0.8	1.2	139	115	**1.1**	0.8	1.4	215	188	**1.0**	0.8	1.2	92	88	**1.0**	0.7	1.4	262	215	**1.0**	0.8	1.3
Social services	98	95	**1.0**	0.7	1.3	50	52	**0.9**	0.6	1.4	48	43	**1.0**	0.6	1.5	39	45	**0.9**	0.6	1.3	59	50	**1.0**	0.7	1.5
Membership organizations	37	35	**0.9**	0.6	1.5	16	15	**1.0**	0.5	1.9	21	20	**0.9**	0.5	1.8	18	19	**0.9**	0.5	1.7	19	16	**1.0**	0.5	2.0
Engineering and management services	97	75	**1.1**	0.8	1.5	42	40	**1.0**	0.6	1.5	55	35	**1.3**	0.9	2.0	33	34	**0.9**	0.5	1.4	64	41	**1.3**	0.9	2.0
Private households	31	54	**0.6**	0.4	0.9	24	31	–	–	–	7	23	–	–	–	16	30	**0.6**	0.3	1.0	15	24	**0.6**	0.3	1.2
Services, not elsewhere specified	23	20	**1.0**	0.5	1.8	4	13	–	–	–	19	7	–	–	–	8	11	–	–	–	15	9	–	–	–
Public administration																									
Executive, legislative and general	30	27	**0.9**	0.5	1.5	12	15	**0.6**	0.3	1.4	18	12	**1.2**	0.6	2.6	10	9	–	–	–	20	18	–	–	–
Justice, public order and safety	33	19	**1.6**	0.9	2.9	11	13	–	–	–	22	6	–	–	–	7	10	–	–	–	26	9	–	–	–
Administration of human resources	34	23	**1.3**	0.8	2.2	15	9	–	–	–	19	14	–	–	–	15	5	–	–	–	19	18	–	–	–
Environmental quality and housing	13	11	**1.0**	0.5	2.3	6	7	–	–	–	7	4	–	–	–	4	4	–	–	–	9	7	–	–	–
Administration of economic programs	13	12	**1.0**	0.5	2.3	8	9	–	–	–	5	3	–	–	–	3	5	–	–	–	10	7	–	–	–
National security and international affairs	39	23	**1.7**	1.0	2.9	30	8	–	–	–	9	15	–	–	–	10	6	–	–	–	29	17	–	–	–
Nonclassifiable establishments	37	27	**1.2**	0.7	2.0	13	12	**0.9**	0.4	2.0	24	15	**1.4**	0.8	2.8	10	4	–	–	–	27	23	–	–	–

[a] Reference group for each industry is composed of women who never worked in that specific industry; ORs were only calculated if at least 10 cases and 10 controls reported working in the category within each stratum.

[b] Adjusted for age; geographic site; age at first birth; number of live births; and level of education.

not found to be at increased risk [29, 33]. Although some studies suggest that this relationship is limited to post-menopausal women [32], we observe this association even when our population was restricted to pre-menopausal women (88.7% of total study population, data not shown). Among parous women, *teachers, librarians and counselors* were at significantly increased risk, while among nulliparous women there was no association. The increased risk estimates were essentially the same for all parous women when further stratified by early and late age at first birth (data not shown). In our study, risk was strongest among *teachers, librarians or counselors* who were employed in these occupations for less than five years; increased risk associated with short job duration may indicate that the occupational exposure is acting as a tumor promoter. To our knowledge, we are the first study to present risk estimates for short-term employment in this occupational group.

Elevated occupational breast cancer risk has often been attributed to reproductive characteristics. In the absence of confounding, parity-specific risk estimates would not be expected to differ from that of all women combined. This was the case for many occupations. Furthermore, risk may differ according to parity status. For all women combined, *natural scientists and mathematicians* were at a decreased risk of breast cancer, however among parous women, no risk was observed and among nulliparous women, the decreased risk became stronger and statistically significant. These stratified analyses do not provide support for the argument that increased risk associated with various occupations is due to uncontrolled confounding by reproductive status. It should be kept in mind that the majority of nulliparous women were still of childbearing age and represented only 24% of the study population, which resulted in small cell sizes. These findings need to be replicated in study populations with more nulliparous women.

Jobs held in electrically related industries such as electrical workers, electrical engineers, electrical technicians, telephone installers, and line workers may expose women to various levels of EMFs [34], which have been hypothesized to increase breast cancer risk [35]. Occupations in other industries that may also involve potentially elevated EMF exposures, such as telephone operators, data entry workers, and computer operators and programmers [34] as well as airline attendants [36]. A comprehensive review of the few existing studies of occupational EMF and breast cancer suggests that a relationship exists [37], although a recent case–control study of occupational EMF exposure found little evidence of such an association [5]. EMF exposure could occur among several occupations reported by women in our study, including *computer and peripheral equipment operators*; *communications equipment operators*; and *secretaries, stenographers and typists* as well as the industries *electronic and other electric equipment*; *electric, gas and sanitary services* and *air transportation*. Yet we found no substantial elevation in the risk estimates for having ever worked in many of these categories, except for the increased risk associated with working as a *computer and peripheral equipment operator* or in the *electric, gas and sanitary services* industry. Without a measure of the actual EMF exposure, it is difficult to draw any conclusions about the association between this occupational exposure and breast cancer, however our study provides only weak support for this hypothesis. Furthermore, potential exposure to EMF through electric blanket use was not associated with breast cancer risk in our study population [18].

As part of this study detailed information on the three longest held jobs as well as on established and potential breast cancer risk factors from a large population-based group of young women was collected and included in these analyses. Thus it is unlikely that these risk factors account for the observed occupation-breast cancer associations although residual confounding remains a possibility. The detailed information collected on job title, usual activities or duties performed, and what the company made or did allowed an industrial hygienist to uniformly code both occupation and industry according to the 1987 SIC and 1980 SOC codes, which group occupations according to the nature of the work performed [20, 21]. To conduct meaningful statistical analyses, initially assigned SIC and SOC codes were collapsed to create as distinct categories as possible with respect to potential occupational exposures while maintaining sufficient cell sizes.

The detailed job history enabled us to examine breast cancer risk not only in relation to ever having worked in a particular occupation or industry but also in relation to duration of employment and the latency (*i.e.*, the time between starting a job and the reference date). This is contrast to several previous studies that only examined breast cancer risk in relation to the longest held or usual job [26, 29, 32]. The use of longest held job could bias associations toward the null since the reference group may include women employed in the occupation for a shorter period. Our ability to examine occupation categorized by job duration allowed us to reduce the likelihood of misclassification since our reference group was restricted to women who did not report the job as one of their three longest held.

Each job reported by a participant was represented in the dataset by a SIC/SOC pair. Due to the number of jobs reported, a large number of occupation/industry

combinations resulted and it was not practical to include both occupation and industry together in the analytic models. Since each occupation or industry category was examined separately, it is possible that estimates of effect were diluted because women included in the unexposed group may have actually had exposures from jobs they held in other occupational or industrial categories similar to the women in an exposed group. For example, 78.3% of the jobs assigned to the occupational category of *teacher, librarian or counselor* were also assigned to the industrial category of *educational services*. Yet, of the jobs assigned to *educational services*, only 57.8% were also assigned the occupation code for *teacher, librarian or counselor*. The association between working in the *educational services* industry and breast cancer risk was essentially null, which may be because several low-risk occupations, such as *executive, administrative and managerial* and *secretaries, stenographers and typists*, also fell under this industrial category.

Several limitations traditionally associated with occupational epidemiologic studies should be considered with respect to our results. For those occupational and industrial categories for which we observed reduced or no risk of breast cancer, we cannot rule out the possibility that less breast cancer may be observed in a particular occupation or industry because women may self-select themselves out of the jobs that involve carcinogenic exposures. Although a wide range of occupations and industries were reported in this study, the number of study participants who worked in any one job or industry tended to be small, limiting our ability to clearly identify relationships between a particular occupation (or industry) and breast cancer risk. In addition, only information on the three longest held jobs was ascertained, so short-term jobs that could have acute but conceivably, adverse occupational exposures were not necessarily accounted for in these analyses. Statistically significant findings could be due to the large number of comparisons that were conducted. It should be noted that none of the study participants reported housewife as one of their three longest held jobs, most likely due to the design of the questionnaire's occupational history section. It is possible that the 24 women who reported that they were never employed for six months or longer were solely housewives. Since we do not have this information, we could not conduct analyses that excluded housewives as has commonly been done in studies of occupation and breast cancer risk [29]. Exclusion of the women who never worked did not alter the results. The use of a single reference group of 'occupationally unexposed' women would ensure comparability of ORs and avoid possible residual confounding. However, in this population, the use of a single reference group was not possible given the small number of women who reported never having worked more than 6 months.

Occupational exposures in relation to cancer have, until recently, been primarily studied among men [38]. To our knowledge, we are among the first population-based case–control studies to examine occupational history and breast cancer risk in women 20–44 years of age, with the ability to take a wide array of breast cancer risk factors into consideration. Case–control studies such as ours are essential for identifying potential occupations and industries that put women at increased breast cancer risk, but these studies cannot pinpoint the particular exposures underlying the association. Job exposure matrices have been used in some studies to better elucidate the occupational exposure-breast cancer risk relationship [39, 40], and future case–control research efforts should consider employing advanced exposure assessment techniques [41]. To better identify job-related breast cancer risk factors, however, occupational cohort studies that collect detailed information on exposures received at work in addition to comprehensive information on established and putative breast cancer risk factors need to be undertaken.

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ELSEVIER

Characteristics of Pubertal Development in a Multi-ethnic Population of Nine-year-old Girls

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PURPOSE: Early age at menarche increases future disease risk. Secular decline in age at menarche has been attributed to body size characteristics, diet, and energy expenditure. Risk factors for puberty have been less frequently explored.
METHODS: A cross-sectional study of 186 New York Metropolitan Area, 9-year-old girls (54 African-American, 70 Hispanic, 62 Caucasians) used interviewer-administered questionnaires to assess exposures. Height and weight were measured. Pediatricians assessed pubertal development according to Tanner stages.
RESULTS: African-Americans were more likely than Caucasians to have achieved puberty as determined by breast or hair development (stage 2 or higher) [age-adjusted odds ratios and 95% confidence intervals = 4.91 (2.15–11.19) and 4.25 (1.85–9.77), respectively]. Pubertal development was similar among Hispanics and Caucasians. Adiposity and height were significantly positively associated with breast or hair development. More sedentary activity hours non-significantly increased the likelihood of hair development. Lower energy, but higher polyunsaturated fat, consumption were suggestive of an association with breast development. Vitamin C and hair development were inversely related. No other nutrients or physical activity measures were related to pubertal development.
CONCLUSIONS: Results are consistent with height and adiposity being associated with pubertal development. Sedentary activity or diet might possibly influence maturation.
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KEY WORDS: Puberty, Body Size Characteristics, Physical Activity, Diet, Cross-sectional, Menarche, Adolescence.

INTRODUCTION

Puberty, characterized by the development of secondary sexual characteristics, begins approximately 3 years before menarche. Pubertal onset is modestly correlated with age at menarche (1, 2). Early maturation has been linked to adverse health outcomes including insulin resistance, breast cancer, and cardiovascular disease (3, 4). Age at menarche varies by geography (5), has declined secularly (6), and differs by race/ethnicity (7). Similar trends, though not well documented, may exist for age of pubertal onset (8). A recent study of over 17,000 US girls found that African-American girls began menses approximately 8.5 months earlier than white girls; pubertal breast and hair development began on average 1 and 1.5 years, respectively, earlier in African-American girls (7). Mexican-American girls are believed to have similar or slightly later reproductive development than Caucasian girls (9). Yet little published information on maturation in other US Hispanics is available. As reproductive characteristics such as birthweight differ among Hispanic subgroups, it is plausible that reproductive development also varies (10).

Acknowledged disparities in the age at menarche imply that environmental factors influence reproductive development, but determinants of earlier maturation are unclear. Adiposity has been consistently, positively associated with onset of menses (11–13). Other factors, including height, diet, and physical activity, have also been linked with menarche, though less consistently (14–18). Whether these characteristics affect pubertal development is unknown (13, 15, 19). We undertook a study of African-American,

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Selected Abbreviations and Acronyms

wt/ht = weight divided by height
BMI = body mass index (weight in kilograms divided by height in meters squared)
Kg = kilograms
YAQ = Youth/Adolescent Food Frequency Questionnaire
MET = metabolic equivalent
kcal/wk = kilocalories per week
ORs = odds ratios
CIs = 95% confidence intervals
aOR = age-adjusted odds ratio

Hispanics, and Caucasian girls to examine pubertal development in relation to body size, physical activity, and diet.

METHODS

A cross-sectional study was undertaken in New York City from Spring 1997 to Fall 1998. Nine-year-old girls of African-American, Hispanic, or Caucasian race/ethnicity, visiting the Mount Sinai Hospital Pediatric Clinic or a nearby pediatric private practice for a wellness visit were eligible. Girls with existing endocrine disorders were ineligible. Of 224 girls invited to participate, 200 (89%) were eligible, agreed to do so, and had either parental or guardian-signed informed consent. Refusal (n = 20) was the primary reason for non-participation. The Mount Sinai Institutional Review Board approved the study protocol.

Classification of Pubertal Development

Girls and their pediatricians assessed the stages of breast and pubic hair development, using standardized drawings and descriptions based on Tanner criteria (provided by Professor Richard Udry, Carolina Population Center, Chapel Hill, NC) (20). These two assessments on a subset (n = 140) were weakly correlated; thus, the physicians' classification of puberty stage was utilized. The lower reliability of self vs. physician assessment of Tanner stage has been previously noted (21). Girls were considered prepubertal (stage 1) or pubertal (stages 2–5) for breast and pubic hair development.

Body Size Characteristics

Pediatric nurses measured height and weight. Weight in kilograms (kg), weight/height (wt/ht), body mass index (BMI; weight (kg)/height in meters squared), and a standardized BMI index were used to examine adiposity. Wt/ht rather than BMI may be a better measurement of childhood obesity (22). BMI is presented to allow for comparison with other published findings. BMI was standardized using the National Health and Nutrition Examination Surveys I and II data (BMI mean and standard deviation are 17.3 and 3.1, respectively, for 9-year old girls) and an index was created: normal (< 85th percentile), at risk of being overweight (85th–95th percentile), and overweight (95th+ percentile) (23–26).

Dietary Intake

Interviewers administered the Youth/Adolescent Food Frequency Questionnaire (YAQ) to assess usual diet and vitamin use in the year preceding interview (27). Average daily nutrient intakes of macronutrients and selected micronutrients (crude fiber, folate, retinol, carotene, and vitamins A, C, D, and E) were calculated by Harvard University using their nutrient/food composition database.

Physical Activity

Girls reported the hours per a typical week they usually spent engaging in a list of pre-specified activities, which were grouped during data analysis by intensity level or metabolic equivalent (MET) scores (28). One MET is equivalent to the oxygen consumption at rest [~1 kilocalorie/kilogram/hour (kcal/kg/hr)]. Adult norms were used because to our knowledge none exist for children. Activities were grouped as follows: sedentary ("jacks, quiet games", "cards, board games", "television/videos/movies", "computer games"); moderate ("walking/hiking"); and vigorous ("jogging/running/track", "soccer/softball/basketball", "swimming/aerobics", "gymnastics/dance class", "bicycling/tennis/skiing"). Other activities were assigned in a similar fashion.

Sedentary, moderate, vigorous, and total (moderate plus vigorous) activity were considered separately. Non-sedentary activity was examined as kcal/wk, as individuals of differing body weights expend different amounts of energy for the same quantity of activity. Total activity (kcal/wk) was calculated as follows (28):

$$total\ kcal/wk_{activity} = [(I_{moderate} \times H_{moderate}) + (I_{vigorous} \times H_{vigorous})] \times Wt$$

where,

H = Hours of activity per week

I = Average MET score by category; moderate (4 kcal/kg· hr), vigorous (7 kcal/kg· hr)

Wt = Body weight in kgs

Other Measures

Race/ethnicity, medical history, birth information, maternal birthplace and education were also collected. Maternal education, less than 12 years vs. 12 or more years, was a proxy for socioeconomic status. Girls self-identified race/ethnicity as African-American, Hispanic, or Caucasian. Those reporting

both African-American and Hispanic (n = 3) were considered African-American (7).

Statistical Analysis

To examine demographic characteristics by pubertal status the Wilcoxon rank-sum (29) and the Mantel-Haenszel chi-square tests were used (30). Unconditional logistic regression was used to determine odds ratios (ORs) and 95% confidence intervals (CIs) (31, 32). Models included age (continuous) and the indicator variable race/ethnicity (Hispanic/African-American/Caucasian). Because height and wt/ht slightly altered risk estimates, the adjusted models are presented. The standard multivariate and residual nutrient methods yielded similar results; hence the models adjusting for caloric intake (continuous) are presented (22). Continuous variables were tertiled based on the study population distribution and were entered as indicator variables. To assess linear trend, indicator variable scores were entered as ordinal. Subgroup analyses were not performed due to the small sample size.

Of the 192 girls with pubertal staging, six were missing body size information. The study population presented consists of 186 girls with pubertal staging, physical activity, and body size data. Girls without dietary information (n = 14) were included in non-dietary analyses as excluding these girls did not materially change estimates. Exclusion of 13 girls whose daily caloric intake was greater than 5,000 kcal (none reported less than 500 kcal) did not alter any of the dietary results; therefore data from the larger group are presented (27).

RESULTS

Figure 1 displays the distributions of breast and hair Tanner stage; more girls were considered pubertal for breast (52%) than for pubic hair development (32%). Pubertal girls were slightly older and their mothers were less educated than prepubertal girls (Table 1). Of 186 girls, 54 were African-American, 70 were Hispanic, and 62 were Caucasians. Among mothers of Hispanic girls, 59% were US born, 26% were born in Puerto Rico, 10% were born in the Dominican Republic, and 5% were born in other Hispanic countries (data not shown). Almost 20% of the African-American mothers were born in the Caribbean Islands. Maternal education was strongly associated with race/ethnicity (data not shown: $\chi^2_{\text{p-value}} < 0.0001$); therefore only race/ethnicity was considered in subsequent analyses.

African-American girls were more likely to have achieved puberty as determined by breast [age-adjusted odds ratio (aOR) and CI = 4.91 (2.15–11.19)] or hair [aOR and CI = 4.25 (1.85–9.77)] development than Caucasian girls, whereas development was similar for Hispanics and Caucasian girls (Hispanic vs. Caucasian aORs and CIs = 1.14 (0.57–2.29) and 1.61 (0.70–3.68) for breast and hair, respectively) (Table 1). African-American girls were slightly older and taller than the other girls, yet median weight and wt/ht were highest among Hispanic girls (all p-values > 0.05) (data not shown). Nearly a quarter of the African-American and Hispanic girls, but only one-tenth of the Caucasian girls, were classified as overweight (data not shown).

As shown in Table 2, pubertal girls were taller, heavier, and had higher wt/ht than pre-pubertal girls for both breast

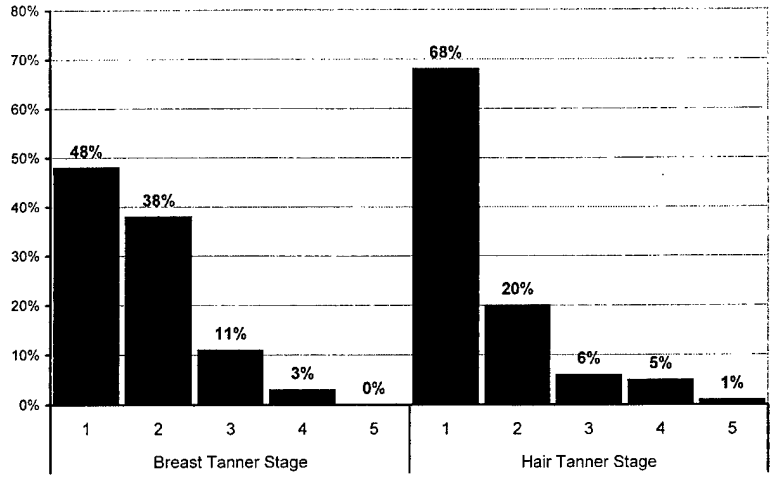

FIGURE 1. Distribution of breast and hair tanner stage among 186 nine-year-old girls in New York City, 1997–1998.

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TABLE 1. Demographic characteristics by pubertal status among 186 nine-year-old girls in New York City, 1997–1998

	Breast				Hair			
	Pre-pubertal	Pubertal			Pre-pubertal	Pubertal		
Number	89	97			127	59		
			p-value*				p-value*	
Age (years, median)	9.42	9.57	0.02		9.46	9.61	0.03	
Maternal education (years, median)	15	12	< 0.01		14	12	0.04	
			aOR†	95% CI‡			aOR†	95% CI‡
Race								
Caucasian (No.)	37	25	1.00		50	12	1.00	
African-American (No.)	12	42	4.91	2.15–11.19	26	28	4.25	1.85–9.77
Hispanic (No.)	40	30	1.14	0.57–2.29	51	19	1.61	0.70–3.68

*P-value for median comparison using the Wilcoxon rank-sum test.
†Age adjusted odds ratios (aORs).
‡Confidence intervals (CIs).

and pubic hair development. Age- and race/ethnicity-adjusted ORs and CIs for pubertal breast development were 6.43 (2.75–15.02) and 4.55 (1.93–10.71) for highest vs. lowest tertile of wt/ht and of height, respectively. The corresponding wt/ht and height ORs and CIs for hair puberty were 3.57 (1.53–8.35) and 5.81 (2.34–14.33). Weight risk estimates were similar to those for wt/ht. Simultaneous consideration of height and wt/ht attenuated the estimates, yet each remained independently related to breast development (data not shown); however, wt/ht was no longer significantly associated with pubertal hair stage. Overweight and at risk of being overweight girls were more likely to have achieved breast puberty, whereas only overweight girls were at greater risk of pubertal hair development.

Pubertal development was similar for girls who engaged in higher vs. lower levels of total physical activity (Table 3);

TABLE 2. Age and race/ethnicity adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for pubertal breast and hair development associated with anthropometric characteristics, among 186 nine-year-old girls in New York City, 1997–1998

	Breast				Hair			
	Pre-pubertal	Pubertal			Pre-pubertal	Pubertal		
Characteristics	No. 89	No. 97	OR	95% CI	No. 127	No. 59	OR	95% CI
BMI (kg/m^2)								
<16	40	22	1.00		48	14	1.00	
16–19	31	31	2.15	0.98–4.71	45	17	1.46	0.62–3.43
>19	18	44	5.13	2.24–11.74	34	28	2.78	1.22–6.33
p-trend*			<0.01				0.01	
Height (in)								
<53	39	18	1.00		47	10	1.00	
53–55	32	36	2.70	1.22–5.97	55	13	1.10	0.43–2.83
>55	18	43	4.55	1.93–10.71	25	36	5.81	2.35–14.33
p-trend			<0.01				<0.01	
Weight (kg)								
<30	41	21	1.00		49	13	1.00	
30–37	33	28	2.09	0.95–4.63	47	14	1.26	0.52–3.06
>37	15	48	6.96	2.93–16.52	31	32	3.58	1.56–8.25
p-trend			<0.01				<0.01	
Weight/height								
<57	41	21	1.00		50	12	1.00	
57–67	32	30	2.22	1.01–4.89	44	18	1.93	0.80–4.65
>67	16	46	6.43	2.75–15.02	33	29	3.57	1.53–8.35
p-trend			<0.01				<0.01	
Standardized BMI index†								
Normal	75	61	1.00		99	37	1.00	
At risk of being overweight	5	10	2.83	0.87–9.18	11	4	0.99	0.29–3.44
Overweight	9	26	3.62	1.48–8.86	17	18	2.52	1.11–5.70
p-trend			<0.01				0.03	

*Indicator variable scores were entered as ordinal to test for a linear trend.
†See Methods section, body size characteristics.

TABLE 3. Adjusted* odds ratios (ORs) and 95% confidence intervals (CIs) for pubertal breast and hair development associated with physical activity, among 186 nine-year-old girls in New York City, 1997–1998

	Breast				Hair			
	Pre-pubertal	Pubertal			Pre-pubertal	Pubertal		
	No. 89	No. 97	OR*	95% CI	No. 127	No. 59	OR*	95% CI
Sedentary (hrs/wk)								
≤13.50	31	29	1.00		45	15	1.00	
13.51–24.50	28	36	1.35	0.60–3.04	43	21	1.49	0.59–3.76
>24.51	30	32	0.93	0.38–2.26	39	23	1.96	0.78–4.94
p-trend†			0.89				0.16	
Total (kcal/wk)‡								
≤1,218	27	35	1.00		42	20	1.00	
1,218–2,548	32	29	0.97	0.44–2.15	44	17	0.65	0.27–1.57
>2,548	30	33	0.89	0.39–2.02	41	22	1.04	0.45–2.40
p-trend			0.78				0.94	

*Adjusted for age, race/ethnicity, height, and wt/ht.
†Indicator variable scores were entered as ordinal to test for a linear trend.
‡Moderate and vigorous total activities.

upper vs. lowest tertile of total activity adjusted-ORs and CIs were 0.89 (0.39–2.02) and 1.04 (0.45–2.40), for breast and hair, respectively. There was no evidence of an inverse trend. Separately considered, neither vigorous nor moderate activity was associated with pubertal development (data not shown). Girls engaging in more sedentary activity may be at increased risk of pubertal hair development [adjusted OR and CI for the upper vs. lower tertile of sedentary activity hours = 1.96 (0.78–4.94)]; risk increased, non-significantly, for each successive tertile of sedentary activity. Further adjustment for total physical activity did not materially alter risk estimates (data not shown). Sedentary activity was not associated with breast development.

Dietary associations are displayed in Table 4. Girls in the upper tertiles of total caloric intake had a lower risk of breast development than the reference group. This inverse trend was borderline significant. There was a suggestion that higher polyunsaturated fat consumption increased the risk of breast development (p-trend = 0.05). No other macronutrients were related to pubertal development. Of the micronutrients, there was a strong inverse association between vitamin C and the risk of being pubertal hair development [adjusted OR and CI for the highest tertile of intake = 0.20 (0.07–0.63); p-trend = < 0.01]. Higher intakes of several other micronutrients may lower the risk of pubertal development, yet many of these estimates were unstable with no clear dose–response.

DISCUSSION

Our study is among few that have examined early pubertal development, and is the first to do so among African-American, Caucasian, and Hispanic girls. A large percent of our population had Caribbean maternal ancestry, another unique study feature. Indeed, the percent of our girls with ancestry in the Caribbean Islands may be larger, because the only information available on the girls' ancestry was maternal birthplace. Advanced breast and hair pubertal status was more common among older girls as well as among African-American girls, but was similar among Hispanic and Caucasian girls. Additionally, girls who were taller, heavier, or had a greater ht/wt ratio were at higher risk of pubertal development. Girls engaging in more hours of sedentary activity had an elevated, non-significant, risk of hair development, yet the data did not support a relation between the other activity measures and pubertal development. Our results suggest a possible relation between some dietary factors and pubertal status. Risk of pubertal breast development was greater among girls with higher polyunsaturated fat intake and among those with lower caloric intake. In contrast, higher vitamin C consumption decreased the risk of hair development.

Advanced pubertal development among African-American girls relative to Caucasian girls agrees with previous studies (7, 33). Differences remained following adjustment for age, height, wt/ht, calories, and polyunsaturated fat (breast only) or vitamin C (hair only), suggesting that genetic or other environmental factors should be considered (34). Whereas we noted similar pubertal status among Caucasian and Hispanic girls, a prospective study in California observed a similar age at menarche for African-American and Hispanic girls which was earlier than the age at menarche for non-Hispanic Caucasians (35). Although not specified, the Hispanic girls in California are presumably of Mexican descent, while ours were predominantly of Caribbean descent. Reproductive development may differ among Hispanic subgroups. It is also possible that risk factors for the puberty and menarche differ because the ages at onset of these two events are strongly, but not perfectly, correlated (36).

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TABLE 4. Adjusted* odds ratios (ORs) and 95% confidence intervals (CIs) for pubertal breast and hair development associated with tertiles of average daily dietary intake among 172 nine-year-old girls in New York City, 1997–1998

	Breast				Hair			
	Pre-pubertal	Pubertal			Pre-pubertal	Pubertal		
Dietary intake	No. 89	No. 97	OR*	95% CI	No. 127	No. 59	OR*	95% CI
Calories (kcal†)								
≤2,330.75	20	37	1.00		38	19	1.00	
2,330.76–3,304.28	33	25	0.30	0.12–0.73	42	16	0.72	0.29–1.79
>3,304.29	26	31	0.42	0.16–1.09	35	22	1.16	0.46–2.91
p-trend‡			0.08				0.74	
Protein (g†)								
≤87.54	21	36	1.00		40	17	1.00	
87.55–120.06	33	25	0.46	0.17–1.28	39	19	1.62	0.58–4.57
>120.07	25	32	1.46	0.35–6.11	36	21	2.86	0.68–12.07
p-trend			0.70				0.15	
Carbohydrate (g)								
≤324.71	23	34	1.00		37	20	1.00	
324.72–446.08	29	29	0.97	0.35–2.64	42	16	0.80	0.28–2.31
>446.09	27	30	2.05	0.40–10.41	36	21	1.82	0.36–9.31
p-trend			0.49				0.59	
Total fat (g)								
≤72.24	22	35	1.00		37	20	1.00	
72.25–108.52	28	30	0.61	0.22–1.69	39	19	0.71	0.25–2.01
>108.53	29	28	0.93	0.12–4.35	39	18	0.81	0.16–4.01
p-trend			0.81				0.73	
Saturated fat (g)								
≤27.64	22	35	1.00		38	19	1.00	
27.65–42.20	26	32	0.54	0.20–1.48	38	20	0.81	0.29–2.25
>42.21	31	26	0.30	0.07–1.29	39	18	0.71	0.17–3.01
p-trend			0.11				0.64	
Monounsaturated fat (g)								
≤29.27	22	35	1.00		37	20	1.00	
29.28–44.00	28	30	0.65	0.24–1.81	38	20	0.73	0.26–2.06
>44.01	29	28	0.83	0.17–4.02	40	17	0.48	0.09–2.49
p-trend			0.73				0.39	
Polyunsaturated fat (g)								
≤14.93	23	34	1.00		41	16	1.00	
14.94–21.80	27	31	1.05	0.41–2.73	36	22	2.46	0.89–6.76
>21.81	29	28	1.21	0.28–5.08	38	19	3.17	0.66–15.10
p-trend			0.05				0.11	
Crude fiber (g)								
≤4.95	24	33	1.00		39	18	1.00	
4.96–6.98	25	33	1.45	0.59–3.55	37	21	1.83	0.72–4.65
>6.99	30	27	1.02	0.31–3.64	39	18	1.23	0.35–4.32
p-trend			0.89				0.64	
Vitamin A (IU†)								
≤7,938.36	20	37	1.00		36	21	1.00	
7,938.37–13,287.28	27	31	0.70	0.27–1.80	38	20	0.96	0.38–2.42
>13,287.29	32	25	0.75	0.28–2.02	41	16	1.16	0.42–3.20
p-trend			0.60				0.78	
Folate (μg†)								
≤361.24	18	39	1.00		32	25	1.00	
361.25–543.01	28	30	0.57	0.23–1.43	38	20	0.57	0.23–1.45
>543.02	33	24	0.62	0.22–1.70	45	12	0.42	0.14–1.23
p-trend			0.38				0.11	
Retinol (IU)								
≤2,266.56	16	41	1.00		35	22	1.00	
2,266.57–4,078.46	29	29	0.62	0.23–1.65	35	23	1.84	0.70–4.85
>4,078.46	34	23	0.52	0.20–1.38	45	12	0.94	0.34–2.58
p-trend			0.21				0.78	

Continued

TABLE 4. Continued

	Breast				Hair			
	Pre-pubertal	Pubertal			Pre-pubertal	Pubertal		
Dietary intake	No. 89	No. 97	OR*	95% CI	No. 127	No. 59	OR*	95% CI
Carotene (IU)								
≤4,538.60	22	35	1.00		35	22	1.00	
4,538.61–9,068.57	28	30	0.56	0.23–1.40	41	17	0.49	0.19–1.24
>9,068.58	29	28	0.81	0.31–2.15	39	18	0.85	0.32–2.26
p-trend			0.70				0.71	
Vitamin C (mg‡)								
≤144.43	21	36	1.00		33	24	1.00	
144.44–238.05	30	28	0.64	0.26–1.57	38	20	0.67	0.27–1.62
>238.06	28	29	0.59	0.22–1.60	44	13	0.20	0.07–0.63
p-trend			0.31				<0.01	
Vitamin D (IU)								
≤346.78	17	40	1.00		33	24	1.00	
346.79–549.26	26	32	0.94	0.37–2.41	39	19	1.18	0.46–3.02
>549.27	36	21	0.48	0.17–1.38	43	14	0.89	0.31–2.56
p-trend			0.15				0.79	
Vitamin E (mg)								
≤8.75	18	39	1.00		36	21	1.00	
8.76–16.10	25	33	0.69	0.26–1.81	31	27	1.76	0.67–4.64
>16.11	36	21	0.51	0.19–1.42	48	9	0.59	0.19–1.86
p-trend			0.20				0.31	

*Adjusted for calories, age, race/ethnicity, height, wt/ht. Total caloric intake model not adjusted for calories.
†Abbreviations: kilocalories (kcal); grams (g); milligrams (mg); international units (IU); micrograms (μg).
‡Indicator variable scores were entered as ordinal to test for a linear trend.

The hypothesis that a critical body weight or fatness is required to trigger menarche has not been confirmed (37). But our study, other cross-sectional studies of puberty (13, 33), and several prospective studies of menarche (18, 35, 38–41) have observed a link between body size characteristics and maturation. Since body fat accumulation occurs around the time of puberty it is difficult to disentangle pre- from post-puberty changes even in prospective studies. Post-puberty body size changes would result in an overestimation of the body-size-characteristic–puberty-status associations in our study. Our limited sample size precluded the re-examination of the previously reported finding that the relationship between BMI and breast development was stronger among Caucasian vs. African-American girls (13).

The influence of diet on maturation is suggested by the delayed menses observed in undernourished and anorexic girls (42, 43). Most observational studies (38, 39), including a longitudinal study of over 2000 Canadian girls (17), and several other prospective studies (35, 40, 41) do not provide consistent evidence linking specific nutrients to age at menarche. For example, in contrast to our findings, others report delayed menarche in relation to higher polyunsaturated fat consumption (44) and to lower vitamin C intakes (39). Although not all studies agree (17, 39), weak associations such as those we noted between some micronutrients and pubertal status agree with reports that menarche occurs later in vegetarian girls (15) and among girls with higher fiber intakes (45). Finally, an inverse association between pubertal breast development and caloric intake agrees with the findings of two prospective studies of menarche (35, 39). The association may be partially that overweight girls underreport their dietary intake (35). Indeed, when heavier girls were excluded from the analyses, similar to Koprowski et al., our inverse association was less pronounced (35).

Anthropometric characteristics, physical activity, and diet are strongly intertwined. When intake exceeds expenditure over an extended period, body weight and body fat increase (46). Despite some evidence that diet and physical activity are independently associated with maturation, it is also possible that they operate through their impact on anthropometric characteristics. If anthropometric variables mediate the relationship, adjustment for body size characteristics might obscure the underlying association. ORs were similar with and without adjustment for anthropometric characteristics suggesting that at least some portion of the influence of physical activity and dietary intake on pubertal development is independent of their effects on body size characteristics. Evidence that physical activity may operate partially independent of body size comes from a prospective study of 15 ballet dancers. Menarche occurred in two-thirds of the girls during a hiatus from dancing, although their body composition and weight remained fairly

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stable (47). This and other evidence suggest that gonadotropin secretion, which is thought to be critical in the onset of puberty, may be suppressed during extreme energy deficits (19).

Delayed menarche and amenorrhea have been associated with prolonged vigorous or moderate physical activity (16, 18, 40, 41, 48, 49), although not all studies support such an association (34, 39). With the exception of an increased risk of hair development among more sedentary girls, our physical activity results were essentially null. In accordance with our finding, a previous study reported an earlier menarche among girls spending more time in sedentary activities (44).

Strengths of our study include the outcome and exposure assessments. Pediatrician assessment of pubertal stage was used. Inter-rater reliability between two pediatricians of pubertal staging for 20 girls (kappa 0.78 for breast and 0.69 for pubic hair) was similar to or better than that previously reported (21). Trained nurses measured body size characteristics. The questionnaire included physical activities of varying intensities as well as an open-ended question capturing less common activities. The YAQ had a 1-year reproducibility among 9 to 18 year olds that was comparable to that of other adolescent dietary questionnaires and was unrelated to age or ethnicity (27). Furthermore, our nutrient values, though slightly higher, were consistent with other reports of girls this age (27). The use of tertiles, or ranks, for categorizing exposures reduces misclassification and minimizes the influence of outliers on risk estimates. Even if exposures were adequately measured, it is possible that exposures earlier in life are more relevant to the onset of puberty than the time-frame of our exposure assessment.

Study limitations include the uncertainty about whether the study population is representative of the local community and the cross-sectional design, which precludes examining the temporal sequence between exposures and pubertal development. Post-puberty changes in exposures may bias estimates. For instance, girls progressing through puberty may become self-conscious about their bodies, thereby possibly reducing dietary intake or increasing physical activity. Reporting of post-puberty behavior would bias dietary associations toward, but physical activity associations away from, the null. Race/ethnic-specific attitudes toward these behaviors would yield estimates that were biased differently between the groups.

Maternal education and access to care provide some information on socioeconomic characteristics. This information was limited and could not be distinguished from race/ethnicity. Yet, despite their similarities in the socioeconomic characteristics, African-American and Hispanic girls differed in their pubertal status suggesting that other environmental or genetic characteristics may be instrumental in pubertal development.

Consistent with previous studies, our strongest findings indicate positive associations between pubertal development and adiposity measures as well as height. The links we observed between pubertal development and dietary intake, notably caloric intake, polyunsaturated fat, and vitamin C, should be weighed against the instability of the risk estimates. In addition to the multiple dietary comparisons made, results of previous studies, including several prospective studies of menarche, did not agree with our results, further indicating the tenuous nature of our dietary findings. Difficulties in assessing diet may hamper the ability of all studies to detect such associations. Finally, the notion that girls engaging in more physical activity have delayed maturation is not supported by our results, although physical activity in our sample was clearly not as strenuous as that of ballet dancers (16, 47). We had limited power to detect small associations and to explore ethnic differences. Future longitudinal studies with larger numbers of multi-ethnic girls can expand our work. Given the link between early puberty and/or menarche and disease risk later in life, elucidation of environmental or lifestyle factors influencing maturation may offer young girls the ability to reduce subsequent disease burden.

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An Empirical Investigation of Albert Ellis' Binary Model of Distress

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Abstract

In the current literature, distress is typically described according to a unitary model; high levels of distress are conceptualized as a high level of negative affect while low levels of distress are typically conceptualized as a low level of negative affect. On the other hand, Albert Ellis and some of his rational-emotive & cognitive-behavioral professional colleagues have more recently described distress as a binary construct composed of two different components: functional negative feelings (e.g., sad), and dysfunctional negative feelings (e.g., worthless). In two studies using 55 USA breast-cancer patients, and respectively, 45 Romanian breast-cancer patients, we compared hypotheses derived from unitary and binary models of distress. The results revealed that in a stressful situation (i.e., upcoming breast surgery), high levels of irrational beliefs were associated with high level of both functional and dysfunctional negative feelings, while low levels of irrational beliefs were associated with low level of dysfunctional negative feelings and high level of functional negative feelings. Thus, that support for the binary model of distress was found in both USA and Romanian samples suggests both the robustness and the generalizability of the results. Theoretical and practical implications are discussed.

Key works: distress, unitary and binary model of distress, functional and dysfunctional negative feelings/emotions, cognitive approach

An Empirical Investigation of Albert Ellis' Binary Model of Distress

Emotional distress (negative affect) has been traditionally described as a unitary construct (Russell & Carroll, 1999; Watson & Tellegen, 1999). The unitary view of distress is that distress levels fall along a continuum moving from low to high, regardless of whether one is measuring specific negative affects (e.g., worthlessness, sadness, anxiety, concern) or a general negative affect obtained by summing the scores of specific negative affect items (e.g., McNair, Lorr, & Droppelman, 1971). Typically in the current literature, high distress refers to high levels of negative affect (e.g., high worthlessness, high sadness) while low distress means a low level of negative affect (e.g., low worthlessness, low sadness) (Beck & Beamesderfer, 1974; Shachman, 1983). Specific labels describing apparently distinct negative affects (e.g., depressed vs. sad), are considered: (1) synonyms for the same emotional experience (e.g., depressed and sad are two different labels for the same emotional experience); (2) referring to the same underlying construct (e.g., dysphoric) with labels (e.g., sad vs. depressed) representing differences in intensity (e.g., moving from sad to depressed) (McNair et al., 1971); or (3) qualitatively different negative feelings which can be functional or dysfunctional depending on their intensities (e.g., high sadness and depressed mood are typically considered dysfunctional while low sadness and depressed mood are typically considered functional). The unitary model of distress is readily seen in both pharmacologic (e.g., Elkin, Shea, Watkins et al., 1989) and nonpharmacologic studies (e.g., Hollom, DeRubeis, Evans et al., 1992; Kovacs, Rush, Beck et al., 1981) focused on reducing patient distress. However, despite its wide-spread acceptance, the unitary model of distress has been challenged.

From both a theoretical and practical perspective, the construct of distress can be subdivided according to qualitative properties. Ellis (1994) has described distress incorporating a binary model in the context of rational-emotive & cognitive-behavioral therapy (REBT/CBT). In contrast to the unitary model, the binary model of distress is comprised specifically of qualitatively different functional (e.g., sad, uneasy) and dysfunctional (e.g., worthless, miserable) negative feelings. Whether people's feelings are functional or dysfunctional is determined based on their subjective experiences, associated cognitions (e.g., rational or irrational beliefs), and consequences of these feelings (e.g., behavioral) (Ellis & DiGiuseppe, 1993). Functional negative feelings mean a negative subjective experience, rational beliefs, and adaptive behavioral consequences while dysfunctional negative feelings mean a negative subjective experience, irrational beliefs, and maladaptive behavioral consequences (Ellis & DiGiuseppe, 1993); defined in this way, dysfunctional negative feelings seem to correspond to clinically significant problems (e.g., anxiety, depression, anger, guilt) while functional negative feelings (e.g., concern, sadness) correspond to normal negative reaction in people facing stressful events (e.g., Bonnano, 2004; Ellis & DiGiuseppe, 1993). Functional and dysfunctional negative feelings can independently be of low, medium, or high intensities (Ellis, 1994). The usefulness of the binary model is perhaps best seen in a clinical example. In the surgical setting, it might be functional to feel sad about upcoming surgery, however it might be dysfunctional to feel worthless or indifferent about it. That is, feelings of worthlessness may contribute not only to unnecessary negative subjective experience, but also to inappropriate responses (e.g., self-blame) while having "neutral affect" is likely to reduce the motivational resources to deal with the stressor (Anderson, 1994). On the other hand, although accompanied by a negative subjective experience, sadness might be associated with adaptive coping mechanisms to deal with the stressor (Bonnano, 2004). Therefore, in a clinical setting the binary model suggests focusing interventions on reducing

dysfunctional feelings (e.g., worthlessness) while recognizing the appropriateness of functional negative feelings (e.g., sadness). A unitary model of distress would not discriminate between functional and dysfunctional negative feelings as clinical intervention foci. According to the unitary model, a clinician would presumably work toward reducing both functional (sadness) and dysfunctional (worthlessness) negative feelings simultaneously. Although there is strong evidence to support the clinical efficacy of REBT (e.g., Lyons & Woods, 1991), there are no data to our knowledge confirming or disconfirming the binary model of distress. Moreover, the hypothesis is testable.

According to Ellis' theory (1994), beliefs about the stressful events are the most critical "causes" of negative feelings. Irrational beliefs are defined as beliefs that are unlikely to find objective empirical support, are not pragmatic, and generally reflect demandingness (DEM). DEM refers to absolutist requirements to oneself, others and life conditions and it is expressed in form of "musts", "shoulds", and "oughts. Rational beliefs are defined as beliefs that are likely to find objective empirical support, are pragmatic, and express preferences rather than demands. Originally, it was implied by Ellis, in accordance with the unitary model of distress, that the dysfunctionality of negative feelings was characterized by their intensity: strong feelings (e.g., high worthlessness, high sadness) were dysfunctional and associated with irrational beliefs while less strong feelings (e.g., low worthlessness, low sadness) were functional and associated with rational beliefs (Ellis, 1962; Ellis & Harper, 1961). In the revised version of the theory, Ellis (Ellis, 1994; Ellis & Harper, 1975) made the assertion that there are qualitative differences between certain similar feelings (e.g., depressed/worthless and sad; anxious and concerned/uneasy); while both functional (e.g., sad) and dysfunctional (e.g., worthless) feelings can independently range in intensity from mild to severe, they differ in their quality. In stressful situations, irrational beliefs have been specifically hypothesized to be associated positively with

both functional and dysfunctional negative feelings. In stressful situations, rational beliefs [frequently measured as low score of irrational beliefs (Bernard, 1998)] are hypothesized to be associated positively with functional negative feelings only. In this context we have to mention that the language of emotion used by the general public and even by professionals is often imprecise. Thus, the general public and some professionals might not agree on the meaning of the terminology suggested by Ellis (Ellis & Harper, 1975) to describe functional and dysfunctional negative feelings. However, the terminology is not important; rather its functionality is fundamental (Ellis & Harper, 1975). Functionality of a feeling is primarily related to rational and irrational beliefs as described above, not to its label, although research (e.g., Wallen, DiGiuseppe, & Dryden, 1992) shows that dysfunctional feelings, defined in this way, seem to correspond to clinically significant problems (e.g., anxiety, depression, anger, guilt). Moreover, as we mentioned above, whether people's feelings are functional or dysfunctional may vary also significantly among individuals based on their subjective experiences these feelings, associated cognitions (e.g., irrational beliefs), and consequences of these feelings (e.g., behavioral) (Ellis & DiGiuseppe, 1993); thus, examining the definitions of rational and irrational beliefs, those of functional and dysfunctional feelings, and the relationships among them, these are clearly not tautological definitions. Prior to studying the interesting implications of the qualitative distinction between functional and dysfunctional negative feelings on behavioral outcomes, a rigorous examination of the core assumption of the binary model of distress is necessary. Specifically, the relation between irrational beliefs and functional and dysfunctional negative feelings in a stressful situation needs to be investigated.

A review of the literature reveals relatively little research examining hypothesized relations between irrational beliefs and functional and dysfunctional negative feelings. Cramer (1985) reported that irrational beliefs were positively correlated with both functional and

dysfunctional negative feelings (as described originally by Ellis & Harper, 1975) in the context of imaginal stressful situations. Cramer (1985) interpreted these data as inconsistent with the binary model, and consistent with a unitary view of distress. However, the study did not directly test the binary model for at least two reasons. First, recent REBT theory concerning the binary model (Ellis, 1994) does not posit that irrational beliefs will not be correlated with functional negative feelings. Functional and dysfunctional negative feelings can be positively correlated with irrational beliefs (Ellis & DiGiuseppe, 1993). A more appropriate test would be to compare levels of functional and dysfunctional negative feelings in individuals with high and low levels of irrational beliefs to determine whether feelings differ in these groups. Second, there was no "real" or actual stressful event preceding distress in that study. According to Ellis (1994), emotional responses to imaginal events [as used in the Cramer et al., (1985) study] may not generalize to actual stressful events (e.g., upcoming surgery), as irrational beliefs may not be activated in relatively "safe" imaginal situations.

A second set of experimental studies (Cramer & Fong, 1991; Cramer & Kupshik, 1993) used rehearsal of irrational beliefs to examine their impact on functional and dysfunctional negative feelings (as described by Ellis & Harper, 1975). These studies found that repeatedly rehearsing thoughts or reading sentences containing irrational beliefs increased both functional and dysfunctional negative feelings pertaining to imaginal stressful situations, consistent with a unitary distress model. Similar to the criticism of Cramer (1985) discussed above, these studies also did not use actual stressful events in their tests of relations between irrational beliefs and negative feelings. Also, to our knowledge, there is no data to support the position that verbal rehearsals of irrational beliefs are internalized or believed in by participants. That is, core irrational beliefs may have a different impact on functional and dysfunctional negative feelings than those that are rehearsed under the direction of an experimenter. In addition, it has been

noted that such rehearsal studies may be particularly vulnerable to the effects of study demand characteristics (Cramer & Kupshik, 1993).

A more recent study (David, Schnur, & Belloiu, 2002) has provided additional preliminary support for the binary model of distress. Specifically, the authors found that high levels of irrational beliefs generate dysfunctional negative feelings (i.e., anger, guilt, anxiety, depression) and low levels of irrational beliefs generate functional negative feelings only (i.e., concern, remorse, sadness) in the context of actual remembered stressful events. However, this study is also inconclusive due to its retrospective design. Specifically, participants were instructed to recall stressful events (e.g., performing poorly on an important exam) to provide the event stimulus. Clearly, a prospective approach would be more powerful. In addition, the study used undergraduate psychology students as participants, which may account for the unusually high correlations found between irrational beliefs and dysfunctional emotions (e.g., they might have been aware of the theory under study). Following the same line of preliminary supporting evidence for a binary model of distress, another study (David, Schnur, & Birk, in press) found that arousal level did not differentiate between functional and dysfunctional negative feelings as would be expected from the unitary model; these results suggest that the distinction between functional and dysfunctional negative feelings is not simply in terms of intensity. However, this conclusion might fit only those feelings that involve a high level of arousal (e.g., anxious) not those feelings which do not involve a high level of arousal (e.g., sad) (see also Watson & Tellegen, 1999).

In a review of this literature, Ellis & DiGiuseppe (1993) argued that a principal component analysis would be necessary to adequately test the binary distress model. Specifically, they hypothesized that two principal components would be revealed. The first should demonstrate that high irrational beliefs (low rational beliefs) will be associated with both

high functional and dysfunctional negative feelings. The second principal component should reveal a positive relation between high rational beliefs (low irrational beliefs) and functional negative feelings, and a negative association between high rational beliefs (low irrational beliefs) and dysfunctional negative feelings.

The purpose of the present study was to empirically test divergent predictions based on unitary and binary models of distress among patients scheduled for breast cancer surgery. In the United States of America, more than 150,000 women undergo lumpectomy and mastectomy for breast cancer each year, and hundreds of thousands more undergo similar surgical procedures (i.e., excisional biopsy for definitive diagnosis) (American Cancer Society, 2003). Research with patients awaiting breast surgery for treatment or diagnosis of breast cancer consistently support this time as a period of heightened distress (Carver, Pozo, Harris et al., 1993; Montgomery, Weltz, Seltz et al., 2002; Northouse, Tocco, & West, 1997) and generally, such distress has been associated with poorer postoperative outcomes in various surgical patient samples (Scott, Clum, & Peoples, 1983; Urrutia, 1975). This population, therefore, offers a unique opportunity to investigate relations between irrational beliefs, functional and dysfunctional negative feelings.

The following competing sets of specific hypotheses were tested in the context of impending breast surgery relating to the diagnosis and/or treatment of breast cancer: (1) Based on the binary model of distress, principal components analysis should reveal two principal components. The first should be positively associated with irrational beliefs and also positively associated with all words describing negative feelings. The second principal component should be negatively correlated with both irrational beliefs and a subset of words describing negative feelings (putative dysfunctional negative feelings). The second principal component should also be positively correlated with a subset of words describing negative feelings (putative functional negative feelings). If the unitary model of distress is correct, then we would anticipate a single

principal component positively correlated with irrational beliefs and all words describing negative feelings. (2) Based on the binary model of distress, the level of dysfunctional negative feelings (as defined by the principal component analysis) should be higher in patients reporting high levels of irrational beliefs, and lower in patients reporting low levels of irrational beliefs. It is important to note that based on the binary model of distress, no specific hypotheses regarding levels of functional negative feelings in patients reporting high or low irrational beliefs are made. If the unitary model of distress is correct, then in stressful situations one would anticipate generally high levels of negative feelings in patients with high levels of irrational beliefs, and low levels across all negative feelings in patients with low levels of irrational beliefs. (3) If the binary model is correct, patients reporting low levels of irrational beliefs will have higher levels of functional negative feelings relative to dysfunctional negative feelings in stressful situations. No predictions are made concerning the relation between levels of functional and dysfunctional negative feelings in patients with high levels of irrational beliefs. However, if the unitary model of distress is correct, then patients reporting low levels of irrational beliefs will have generally low levels of negative feelings. Furthermore, according to the unitary model of distress, high levels across all negative feelings should be found in patients with high levels of irrational beliefs.

The present investigation has both theoretical and practical implications. From a theoretical point of view the results should promote better understanding of the concept of distress, either as a unitary or binary construct. From a practical point of view, the results may help guide clinicians to target interventions to control distress in patients awaiting breast cancer surgery.

Method

Participants

USA patients (N=55) scheduled for excisional breast biopsy or lumpectomy in a large USA metropolitan area hospital were consecutively recruited. From the surgical perspective, there is little difference between excisional biopsy and lumpectomy outside the need to take a greater surgical margin with the later (DeVita, Hellman, & Rosenberg, 1997) and therefore, these populations typically are combined together in the same group in clinical research (e.g., Montgomery et al., 2002). No medications were administered until patients reached the operating room. Eligible patients were at least 18 years of age, completed study materials, were not currently pregnant, and had no other concurrent uncontrolled major illness. Fifty-five women (71% scheduled for excisional breast biopsy and 29% for lumpectomy) meeting the above criteria participated. Age ranged from 19 to 72 years (mean age=48.58, SD=13.52). 82% percentage of the sample described themselves as White, 5% as African American, 10% as Hispanic, 1% as Asian, and 2% as other. 57% percent of the sample was currently married and 73% percent had earned at least a college degree. Neither demographic nor medical variables predicted patients' distress (POMS-SV) (p's > .05.), and therefore they were not included in further analyses.

Materials

Profile of Mood States Short Version (POMS-SV) (DiLorenzo, Bovbjerg, Montgomery et al., 1999) is a shortened version of the classic mood adjective checklist (McNair et al., 1971). Strong psychometric properties of the POMS-SV have been found with breast cancer patients (DiLorenzo et al., 1999). Although the patients completed the full version of POMS-SV, the principal component analysis, as well as analyses based on the results of the principal component analysis, used only the 21 emotional items from the tension-anxiety, depression-dejection, and anger-hostility subscales as they were the only items theoretically related to Ellis's cognitive theory of emotions/distress (Ellis, 1994); the subscales of vigor-activity, fatigue-inertia, and

confusion-bewilderment were excluded because they refer more to physiological, cognitive, and behavioral indicators of distress rather than to its emotional components. The analyses of the psychometric subscales investigated in this study show results comparable with previous studies (DiLorenzo et al., 1999).

Common Beliefs Survey-III-Short Form (CBS-III-SF) is the shortened version of the Common Beliefs Survey-III (CBS-III). CBS-III has been used in many studies and proved to have very good psychometric properties (e.g., Thorpe, Parker, & Barnes, 1992; Thorpe, Goeffrey, Walter, et al., 2001). CBS-III-SF (e.g., Thorpe & Frey, 1996) contains 19 items measuring irrational beliefs (IBs) and provides a total score of IBs that served as the measure of IBs in the present study. A high score on the scale indicates a low level of IBs (note: items 4, 11, and 19 are reversed when the total score is computed). Consistent with the large literature in this area (see Bernard, 1998), high IBs were conceptualized as low rational beliefs (RBs); while low IBs were conceptualized as high RBs. The CBS-III-SF has been found to have very good psychometric properties comparable with those of CBT-III (e.g., Thorpe & Frey, 1996).

Procedure

All study measures were administered individually. Both the POMS-SV and CBS-III-SF were included in a take-home questionnaire packet, which patients completed prior to the day of surgery. All participants provided informed consent consistent with IRB guidelines. In addition, five experts from the Albert Ellis Institute provided ratings of the 21 POMS-SV items, related to their functionality and dysfunctionality.

Statistical analyses methods

An alpha level of .05 was used for all statistical tests. In the first phase of the analyses, a principal component analysis (PCA) was performed to test the two component prediction of the binary model of distress. PCA involves a mathematical procedure that transforms a number of

(possibly) correlated variables into a (smaller) number of uncorrelated variables called principal components. If the PCA analysis reveals one component, these results would be consistent with the unitary model; if two components are revealed, the data would be consistent with the binary model suggesting that participants distinguish between words describing functional and dysfunctional feelings. We will not rotate the components because neither an orthogonal nor an oblique rotation could fit the assumptions of the investigated theory. Thus, according to the theory, in the irrational beliefs condition dysfunctional and functional feelings come together, while in the rational beliefs condition functional feelings are not accompanied by dysfunctional feelings. Therefore, neither an orthogonal rotation (forcing a pattern in which functional and dysfunctional feelings are independent) nor an oblique rotation (assuming that functional and dysfunctional feelings are correlated) can test the theory. Rather, an unrotated PCA solution, which aims to reduce the dimensionality of a data set while retaining as much information as is possible and which computes a compact and optimal description of the data set, is the best test for the theory investigated by PCA (e.g., Pedhazur & Schmelkin, 1991). With the two components confirmed, separate total scores for both functional and dysfunctional negative feelings would be computed using items identified in principal component analysis. More precisely, feelings negatively associated with the second component but positively associated with the first component will be used to compute the total score for dysfunctional negative feelings. Feelings positively associated with both components will be used to compute the score of functional negative feelings. The relations between these constructs will be further analyzed. Two possibilities exist. First, functional and dysfunctional negative feelings may refer to the same underlying construct with dysfunctional feelings signifying high level/intensity of feelings and functional feelings referring to a low level of those feelings; according to this view, they would differ in terms of intensity. If this is true, we expect that these feelings will always load on

the same component in the principal components analysis and correlate positively with IBs; more precisely, high IBs will be associated with both high level of functional and high level of dysfunctional negative feelings while low IBs would be associated with both low level of dysfunctional and low level of functional negative feelings. The second possibility is that these two terms may refer to two different constructs [which differ in terms of quality (by their nature)] and each can have low, medium, or high intensities. In this context, if the binary model of distress is correct, functional and dysfunctional negative feelings would then load on two components and high level of IBs will be associated with both high level of functional and high level of dysfunctional negative feelings, while low level of IBs would be accompanied by low level of dysfunctional and high level of functional negative feelings. If, in this context, the unitary model of distress is correct, then again functional and dysfunctional negative feelings would load on one component and high level of IBs will be associated with both high level of functional and high level of dysfunctional negative feelings, while low level of IBs would be accompanied by low level of dysfunctional and low level of functional negative feelings. The results of principal component analysis and between and within group comparisons will be used to test these possibilities. Correlational analyses will complement our mentioned statistical analyses.

Results [1]

In general, IBs (CBS-III-SV) were correlated with distress (POMS-SV) ($r = -0.40$, $p < .01$). Higher levels of distress were associated with higher levels of IBs (note: a low score on the CBS-III-SV represents a high level of IBs).

Principal component analysis.

In the first phase, all items from the "emotional" subscales of POMS-SV (tension-anxiety, depression-dejection, and anger-hostility) and the total CBS-III-SV score were entered

into a principal component analysis. A previous examination of the correlation matrix showed that all linear correlations were significant (all $p < .05$) ranging from plus/minus 0.28 to plus/minus 0.90. In order to simplify the interpretation of the components, the statistical program was set to eliminate any correlations lower than 0.10. The principal component analysis revealed two main components.[2] The first component accounted for 50% of the variance and was named "general stress." This component correlated positively with all negative feelings items and negatively with the score of CBS-III-SV (indicating: higher IBs correlate with higher general stress) (see Table 1). The second component, labeled "functional stress," accounted for 12% of the variance and was positively correlated with the score of CBS-III-SV [indicating: lower IBs correlate with higher functional stress]. Some negative feeling items were positively correlated with functional stress while others were negatively correlated or not correlated at all (see Table 1). Based on the binary model of distress, the negative feelings items from the POMS-SV that were positively correlated with the second component (functional stress) were defined as functional negative feelings; their score was summed to compute the functional negative feelings score. Negative feelings items negatively associated with the functional stress component were defined as dysfunctional negative feelings; their score was summed to compute the dysfunctional negative feelings score.

(Insert Table 1 about here)

The distinction between functional and dysfunctional negative feelings was also examined through the use of expert raters. Five experts from the Albert Ellis Institute (all trained as supervisors in REBT; each with over 15 years of experience) independently rated the POMS-SV items. Specifically, the five experts were asked to classify the negative feeling items into

functional (1) and dysfunctional (0) feeling categories. For an item to meet criterion, all 5 experts had to agree. Results of the principal component analysis and the expert ratings were then compared, revealing concordance across the classification methods (phi=0.75; $p < .01$). Experts classified functional and dysfunctional feelings items in a manner identical to the principal component analysis with two exceptions: (1) the adjective "anxious" was classified as dysfunctional by experts while it appeared as functional in component analysis; and (2) the adjective "annoyed" was classified as functional by experts while it appeared as dysfunctional in component analysis.

In the second phase of the analyses, subscale scores for functional and dysfunctional negative feelings were examined in two ways. First, according to the results of the principal component analysis (see Table 1); all items negatively related to the functional stress (Component 2) were considered dysfunctional negative feelings (alpha Cronbach= 0.78), and those positively related with functional stress were considered functional negative feelings (alpha Cronbach= 0.80). Second, according to the expert ratings, excluding the two items "annoyed" and "anxious" from the previous classification; alpha Cronbach for dysfunctional negative feelings subscale was 0.78, and 0.75 for functional negative feelings subscale.

Analyses of dysfunctional and functional negative feelings identified by principal component analysis.

The correlation between IBs and the dysfunctional negative feelings subscale was $r=-0.50$ ($p < .01$). The correlation between IBs and functional negative feelings was not significant ($p > .05$). To more closely examine these relations and to further test the binary model, patients were divided into high IBs and low IBs groups using the mean (m=63) plus/minus one standard deviation (SD=8) as the cut off points. Between group comparisons revealed that the level of dysfunctional negative feelings was significantly higher in the high IBs group than in the low IBs

group [t (26)=3.4, p< .01]. There was no difference between the levels of functional negative feelings in these two groups (p> .05). Within the IB groups, analyses revealed that the level of functional negative feelings was higher than the level of dysfunctional negative feelings in both the low IBs group [t (13)=-3.5, p< .01] and the high IBs group [t (13)=-2.6, p< .05].[3]

Analyses of dysfunctional and functional negative feelings based on expert ratings.

Using the expert ratings of dysfunctional and functional negative items, the correlation between IBs and the dysfunctional negative feelings subscale was r=-0.43 (p< .01). The correlation between IBs and functional negative feelings subscale was not significant (p> .05).

As above, patients were divided into high IBs and low IBs groups. Again, between group comparisons demonstrated that the level of dysfunctional negative feelings was higher in the high IBs group than in the low IBs group [t (26)=3.2, p< .01]. There was no between group difference in the level of functional negative feelings (p> .05). Within group comparisons revealed that the level of functional negative feelings was higher than the level of dysfunctional negative feelings in both the low IBs group [t (13)=-3.4, p< .01] and high IBs group [t (13)=-2.9, p<.05] .[3]

Thus, whether dysfunctional and functional negative feelings subscales were determined by principal component analysis or experts ratings, the analyses revealed the same pattern of results.

Supplementary analyses

In order to examine the binary model prediction that arousal, which is hypothesized to be related to the intensity of feelings (Schachter & Singer, 1962; 1979; Sinclair, Hoffman, Martin et al., 1994), is similarly related to both functional and dysfunctional negative emotions (as both have low, medium and high level of intensities), we selected the two POMS-SV items from the vigor-activity subscale with the greatest face validity as indicators of physiological arousal (see

also Sinclair et al., 1994): "active" and "energetic". The correlations between these two items and functional and dysfunctional negative feelings are presented in Table 2.

(Insert Table 2 about here)

Discussion

Before further research should directly exploit these findings, it is fundamental to demonstrate the reliability, generalizability, and the robustness of this effect. For example, it is possible that the apparent support of the binary model of distress is only a byproduct/artifact of the method (e.g., small sample size). Moreover, recent studies also suggest the role of culture in shaping feelings and distress. Romanians, for example, have also been shown to differ from Caucasian Americans on a variety of psychological variables (i.e., well-being) that reflect cultural-specific indicators (Frost & Frost, 2000). These variables may be related to the functional–dysfunctional feelings distinction.

Study 2

In order to further examine the reliability, generalizability, and the robustness of the effect found in Study 1, we selected a Romanian sample for Study 2 because previous studies (e.g., Frost & Frost, 2000) had suggested that it might be an important difference between Romanians and Caucasian Americans in variables related to distress (i.e., well-being). In this study, we aim to prove that the distinction between functional and dysfunctional feelings is not an artifact of the methodological issues or a cultural bias but a robust, general, and reliable phenomenon.

Participants

Romanian patients (N=45) scheduled for excisional breast biopsy or lumpectomy in a large Romanian metropolitan area hospital were consecutively recruited. No medications were

administered until patients reached the operating room. Eligible patients were at least 18 years of age, completed study materials, were not currently pregnant, and had no other concurrent uncontrolled major illness. Forty-five women (80% scheduled for excisional breast biopsy and 20% for lumpectomy) meeting the above criteria participated. Age ranged from 19 to 65 years (mean age=42.45, SD=10.12). 95% percentage of the sample described themselves as White, 5% as Gypsies. 62% percent of the sample was currently married, and 50% percent had earned at least a college degree. Neither demographic nor medical variables predicted patients' distress (POMS-SV) (p's > .05.), and therefore they were not included in further analyses.

Materials

We used the materials described in Study 1. All materials were adapted for Romanian population and have proved psychometric properties comparable with those of the English versions (David, 2003).

Procedure

We used exactly the same procedure described in Study 1.

Results [1]

In general, IBs (CBS-III-SV) were correlated with distress (POMS-SV) ($r = -0.38$, $p < .01$). Higher levels of distress were associated with higher levels of IBs (note: a low score on the CBS-III-SV represents a high level of IBs).

Principal component analysis.

The procedure was identical with that used in Study 1. The analysis of the correlation matrix showed that all correlations were significant (all $p < .05$) ranging from plus/minus 0.30 to plus/minus 0.87. The results obtained by using PCA are presented in Table 3.

(Insert Table 3 about here)

As one can see, the results are consistent with those obtained in Study 1 with one notable exception: according to PCA, the item "anxious" seems to be dysfunctional rather than functional.

As in Study 1, the distinction between functional and dysfunctional negative feelings was also examined through the use of expert raters. Three Romanian experts from the Romanian Center for Cognitive and Behavioral Psychotherapies (all Romanian supervisors in REBT; each with over 10 years of experience) independently rated the POMS-SV items. For an item to meet criterion, all 3 experts had to agree on its functionality. Results of the principal component analysis and the expert ratings were then compared, revealing concordance across the classification methods (phi=0.87; $p < .01$). The results were consistent with those of Study 1. Again, experts classified functional and dysfunctional feelings items in a manner identical to the principal component analysis with one exception: the adjective "annoyed" was classified as functional by experts, while it appeared as dysfunctional in component analysis.

Analyses of dysfunctional and functional negative feelings identified by principal component analysis.

The correlation between IBs and the dysfunctional negative feelings subscale (alpha Cronbach=0.76) was $r=-0.49$ ($p < .01$). The correlation between IBs and functional negative feelings subscale (alpha Cronbach=0.75) was not significant ($p > .05$). To more closely examine these relations and to further test the binary model, patients were divided into high IBs and low IBs groups using the mean (m=65) plus/minus one standard deviation (SD=7.4) as the cut off points. Between group comparisons revealed that the level of dysfunctional negative feelings was significantly higher in the high IBs group than in the low IBs group [$t(23)=3.8$, $p < .01$]. There was no difference between the levels of functional negative feelings in these two groups

($p > .05$). Within the IB groups, analyses revealed that the level of functional negative feelings was higher than the level of dysfunctional negative feelings in both the low IBs group [t (12)=-4.3, $p < .01$] and the high IBs group [t (11)=-3.2, $p < .05$].[3]

Analyses of dysfunctional and functional negative feelings based on expert ratings.

Using the expert ratings of dysfunctional and functional negative items, the correlation between IBs and the dysfunctional negative feelings subscale (alpha Cronbach=0.79) was r=-0.40 ($p < .01$). The correlation between IBs and functional negative feelings subscale (alpha Cronbach=0.76) was not significant ($p > .05$).

As above, patients were divided into high IBs and low IBs groups. Again, between group comparisons demonstrated that the level of dysfunctional negative feelings was higher in the high IBs group than in the low IBs group [t (23)=3.6, $p < .01$]. There was no between group difference in the level of functional negative feelings ($p > .05$). Within group comparisons revealed that the level of functional negative feelings was higher than the level of dysfunctional negative feelings in both the low IBs group [t (12)=-3.6, $p < .01$] and high IBs group [t (11)=-2.5, $p < .05$].[3] Thus, whether dysfunctional and functional negative feelings subscales were determined by principal component analysis or expert ratings, the analyses revealed the same pattern of results.

Supplementary analyses

As in Study 1, we selected the two POMS-SV items from the vigor-activity subscale, with the greatest face validity as indicators of physiological arousal (see also Sinclair et al., 1994): "active" and "energetic". The correlations between these two items and functional and dysfunctional negative feelings are presented in Table 4.

General Discussion

To date, empirical research seeking to distinguish between unitary and binary models of distress have used imagined (e.g., Cramer, 1985), verbally rehearsed (Cramer & Fong, 1991), or recalled (David et al., 2000) stressful events. To our knowledge, no study has addressed this question in regard to a current life stressor. The present research investigated the nature of the construct of distress in women facing impending breast surgery. Overall, the present results were consistent with the binary model of distress (Ellis & Harper, 1975, Ellis, 1994) on two levels. First, principal component analysis, in two separate studies, revealed two components, which we labeled general stress and functional stress. General stress was represented by high scores across all words describing negative feelings. It was associated with higher levels of IBs. Functional stress was positively related to a subset of negative feelings words (functional), and negatively related to another subset of negative feelings words (dysfunctional). Experts' ratings also supported this distinction. Lower IBs were also associated with functional stress. These results were consistent with hypotheses for the binary construct of distress. The data clearly supported the position that patients could differentiate between terms describing their functional and dysfunctional feelings. In addition, in both studies, dysfunctional negative feelings were higher among the patients with high IBs compared to those with low IBs. Functional negative feelings did not differ between these groups. Functional negative feelings scores were greater than dysfunctional feelings scores regardless of IB Group. These results uniformly support the binary model of distress. Moreover, this conclusion was supported in both USA and Romanian samples, supporting the generalizability and robustness of the phenomenon.

Supplementary analyses, in both studies, also supported the binary model of distress. Consistent with results published by David et al. (2002), arousal was related to both functional and dysfunctional negative feelings. As arousal has been hypothesized to be primarily related to the intensity of feelings (Schachter & Singer, 1962; Sinclair et al., 1994), the data suggest that

the distinction between functional and dysfunctional feelings is not simply of intensity. Future studies should expand on this line of research to include physiological measures of arousal to further evaluate these possibilities (see also Watson & Tellegen, 1999).

It is interesting to note that in both studies only few feeling items were not consistently categorized by expert REBT raters and principal component analysis. In both studies "annoyance" was defined by raters as a functional negative feeling, while principal component analysis of patients' response revealed that it behaved as a dysfunctional negative feeling. The finding that annoyance might be better classified as a dysfunctional negative feeling is consistent with the results of David et al. (2002). That study demonstrated that annoyance correlated positively with higher IBs. Also, although "anxious" was viewed as dysfunctional by the raters and is generally so viewed in REBT (Ellis, 1994), in our principal component analysis it behaved as a functional negative feeling in Study 1 (USA sample) and dysfunctional negative feeling in Study 2 (Romanian sample). It is tempting to speculate that the meaning of the term anxious may be related to "functional" for USA individuals anticipating surgery (e.g., "anxious" may refer to "being eager to finish surgery" rather than to anxiety) while for Romanian sample its meaning is closer to that of the term "anxiety. However, further study is necessary to clarify this issue.

The present results appear to complement overall movements in affect research. That is, the broader literature has supported both the bipolar (positive and negative affect as bipolar constructs) and independence (positive and negative affect as independent constructs) models of affect (for details and integration of these frameworks see Russell & Carroll, 1999). Based on our own results and this field of affect research, in stressful situations high IBs may be mainly associated with dysfunctional negative feelings, meaning both negative affect/high arousal (e.g., furious) and negative affect/low arousal (e.g., depressed, worthless), in a bipolar framework of affect (Russell & Carroll, 1999). They correspond to high negative affect (e.g., furious) and low

positive affect (e.g., depressed, worthless) in the independence framework (Watson & Tellegen, 1999). On the other side, in stressful situations, low IBs seem to be mainly associated with functional negative feelings (e.g., sadness), meaning negative affect/medium to high arousal, in a bipolar framework (Russell & Carroll, 1999) or unpleasantness in an independence framework (Watson & Tellegen, 1999).

We can see that while high IBs seem to generate feelings with a high or low arousal component, low IBs tend to produce feelings with arousal levels between medium and high. If one accepts the Yerkes-Dodson Law -- the optimum level of performance in complex tasks is met in a medium arousal condition (Yerkes & Dodson, 1908) -- this might explain the functionality of low IBs and dysfunctionality of high IBs. Future works should explore all these relationships in detail, including analyses between specific emotions and specific beliefs.

Overall, these results support the binary model of distress. These findings may thus have important theoretical and practical implications. From a theoretical point of view, the results contribute to the conceptual analysis of distress. Functional and dysfunctional negative feelings may have very different consequences. For example, these data are consistent with a whole line of research in motivation (e.g., Anderson, 1994; Harmon & Mills, 1999; Yerkes & Dodson, 1908) showing that medium to high levels of emotional arousal (including negative feelings) can have functional behavioral consequences (see also, Ellis, 1994). Future research should try to clarify the role of functional negative feelings as a potentially adaptive construct. These results also suggest the potential utility of (re)conceptualizing the theoretical models clinical professionals use to deal with negative affect during stressful events. Trying to reduce negative affect as a whole may make more sense than trying to enhance positive affect during a stressful event (e.g., generally, we don't expect people to experience positive feelings during stressful events). However, trying to reduce the negative affect as a whole during a stressful event might

be inappropriate. Is it adaptive to feel neutral, calm, and relaxed during a stressful event? Having "neutral affect" is likely to reduce the motivational resources to deal with the stressor (Anderson, 1994; Yerkes & Dodson, 1908). Does one want to reduce the negative affect as a whole but only to a point that preserves its motivational valences? If so, we are not aware of any research establishing a certain point below which the negative affect should not be reduced. The present results support a theoretical model which instead suggests the reduction of suffering by reducing dysfunctional negative feelings which may be accomplished while preserving the motivational resources to deal with the stressor by maintaining functional negative feelings. Moreover, this could explain some interesting empirical data showing that depression is associated with immunosuppression but grief (sadness) is not (e.g., Zisook, Shuchter, Irwin et al., 1994).

From a clinical point of view this model may impact on (1) the way distress is targeted by interventions [e.g., in stressful situations clinical professionals might target dysfunctional negative emotions only (e.g., depression) rather than functional negative emotions (e.g., sadness)], and (2) the methodology clinical professionals use to quantify distress (e.g., as functional and dysfunctional negative feelings are two different constructs, we should assess accordingly rather than through the use of unitary distress measures).

The present study, however, is not without its limitations. First, recent research has raised the possibility that IBs and RBs are not bipolar constructs but rather are independent constructs (Bernard, 1998). Low IBs do not necessary mean high RBs. Therefore, the present results should be confirmed using a beliefs scale with separate IB and RB subscales (e.g., Bernard, 1998). Second, the results need to be replicated in various stressor conditions, various modalities of operationalization of the dependent variables (e.g., subjective, behavioral, physiological) and larger groups of participants to formally confirm the stability and generalizability of the findings obtained with the principal component analysis. To attempt do so in this initial study, however,

would have been premature given the lack of prior empirical support for the core assumption of the binary model, namely, that based on rational and irrational beliefs constructs we can differentiate between functional and dysfunctional negative feelings which are qualitatively different. Some confidence of such stability is provided within this study since the results of our principal component analysis were closely related to the independent experts-rating procedure and were consistent with a previously established theoretical model and within two culturally different samples. Third, neither this study nor previous research has established a link between specific reductions in dysfunctional negative feelings and improvement in mental or physical health. Again, to attempt do so in this initial study, however, would have been premature given the lack of prior empirical support for the core assumption of the binary model. Finally, our supplementary analyses about the relationships between functional and dysfunctional feelings and arousal items should be considered only preliminary because the arousal items do not constitute a psychometrically-validated scale in these studies; however, the fact that the results obtained by using these analyses replicated the results of previous publication (e.g., David et al., 2002; David et al., in press) is encouraging in the further exploration of these relationships.

In conclusion, the results of the present study are consistent with the binary model of distress (Ellis & Harper, 1975), with previous theoretical analysis (Ellis & DiGiuseppe, 1994), empirical analyses (e.g., David et al., 2002; David et al., in press) and previous clinical suggestions (Ellis, 1994). The results appear to fit well with the broader frameworks of distress and affect (Russell & Carroll, 1999; Watson & Tellegen, 1999). The present results have both important theoretical (how distress is conceptualized) and clinical (what is targeted for intervention) implications, and being replicated in both USA and Romanian samples, they prove their robustness and generalizability. However, additional studies testing the binary model (Ellis, 1994; Ellis & Harper, 1975) with other stressors and other samples are necessary for definitive

conclusions regarding its validity as compared with the older version of Ellis' unitary model of distress (Ellis, 1962; Ellis & Harper, 1961).

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Footnotes

1 For the sake of brevity we present only the most relevant analyses and results, directly related to our hypotheses. Detailed information about PCA and further analyses is available from the senior author upon request.

2 Two additional components had eigenvalues greater than 1. However, they accounted for little variance (4% and 3% respectively) and were difficult to interpret. Therefore, they were dropped from discussion of the study results.

3 This pattern was replicated when the mean value of the sample was used as the cut-off point for high IBs and low IBs groups rather than the mean plus and minus 1 SD.

Tables

Table 1

The first two components as resulted from the principal component analysis and the correlations between variables and components

	Component 1 General Stress 50% of variance	Component 2 Functional Stress 12% of variance
Blue	.83	.24
Miserable	.82	-.29
Angry	.80	-.25
Unhappy	.80	-
Tense	.77	.32
Sad	.76	.18
Bitter	.75	-.37
Hopeless	.75	-
Uneasy	.74	.49
Resentful	.71	-.23
Discouraged	.70	-
On edge	.70	.45
Helpless	.69	-
Furious	.68	-.51
Anxious	.67	.44
Grouchy	.67	-
Nervous	.66	.54
Worthless	.64	-.52
Restless	.63	.32
Annoyed	.60	-.22
Peeved	.58	-.32
CBS-III-SV	-.42	.29

Note: The correlations lower than 0.10 are not displayed in the table

Table 2

The correlations between arousal items (i.e., active, energetic) and functional and dysfunctional negative feelings as resulted from principal component analysis (PCA) and experts ratings (ER)

	Dysfunctional negative feelings (PCA)	Dysfunctional negative feelings (ER)	Functional negative feelings (PCA)	Functional negative feelings (ER)
Active	.30	.30	.29	.29
Energetic	.37	.37	.47	.48

Note: All correlations are significant at $p < .05$

Table 3

The first two components as resulted from the principal component analysis and the correlations between variables and components

	Component 1 General Stress 48% of variance	Component 2 Functional Stress 16% of variance
Blue	.79	.25
Miserable	.73	-.25
Angry	.78	-.30
Unhappy	.84	-
Tense	.80	.42
Sad	.78	.30
Bitter	.80	-.31
Hopeless	.80	-
Uneasy	.76	.32
Resentful	.77	-.33
Discouraged	.75	-
On edge	.74	.41
Helpless	.65	-
Furious	.78	-.44
Anxious	.77	.-27
Grouchy	.78	-
Nervous	.79	.57
Worthless	.75	-.42
Restless	.68	.28
Annoyed	.75	-.35
Peeved	.78	-.25
CBS-III-SV	-.37	.32

Note: The correlations lower than 0.10 are not displayed in the table

Table 4

The correlations between arousal items (i.e., active, energetic) and functional and dysfunctional negative feelings as resulted from principal component analysis (PCA) and experts ratings (ER)

	Dysfunctional negative feelings (PCA)	Dysfunctional negative feelings (ER)	Functional negative feelings (PCA)	Functional negative feelings (ER)
Active	.34	.31	.30	.33
Energetic	.42	.39	.43	.39

Note: All correlations are significant at $p < .05$

Acculturation and its Relationship to Smoking and Breast Self-Examination Frequency in African American Women

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Abstract

The concept of acculturation has been used to understand differences in health behaviors between and within a variety of racial and ethnic immigrant groups. Few studies, however, have examined the potential impact of acculturation on health behaviors among African Americans. The present study had two goals: 1) to reconfirm relations between acculturation and cigarette smoking; 2) to investigate the impact of acculturation on another type of health behavior, cancer screening and specifically breast self-examination (BSE). African American women (N=66) attending an inner-city cancer-screening clinic completed study questionnaires. Results reconfirmed psychometric properties of the African American Acculturation Scale (AAAS); replicated the negative association between acculturation and lifetime smoking status; and found relations between acculturation and women's adherence to BSE frequency guidelines. Findings from this study raise the possibility that specific aspects of acculturation may better explain specific health behaviors.

Key Words: African American, Acculturation, Breast Self Exam, Smoking

INTRODUCTION

Acculturation refers to the process in which an individual adopts or adheres to attitudes, beliefs, practices, or behaviors congruent with that of the dominant culture (Berry, 1980). Acculturation has been conceptualized as a confluence of traditional rituals and practices, food and activity preferences, ethnic composition of one's interpersonal relationships, values, perceived self-identity, and immigration status variables (e.g., place of birth, generational status in U.S., length of residency). Several measures have been developed to assess acculturation in populations such as Asian Americans (Suinn, Richard-Figueroa, Lew, & Vigil, 1987), Latino Americans (Marin, Sabogal, Marin, & Otero-Sabogal, 1980), and Native Americans (Hoffman, Dana, & Bolton, 1985).

For African American populations, however, acculturation has received little research attention. According to Landrine and Klonoff (1994), the identification of African Americans as a racial group, first, and an ethnic or cultural group, second, may explain the relative delay in exploring acculturation in this population. To date, only two scales have been developed to measure acculturation within the African American population (Landrine & Klonoff, 1994; Klonoff & Landrine, 1999; Snowden & Hines, 1999). Landrine and Klonoff's (1994) scale, the African American Acculturation Scale (AAAS), revised in 2000 (Klonoff & Landrine, 2000), assesses several dimensions of African American culture theoretically derived to reflect the degree of connection an individual has to African American culture as opposed to the dominant culture (i.e., White American culture). Importantly, scores on the separate subscales of the AAAS have not been found to be associated with income, social class, or level of education (Landrine &

Klonoff, 1994). This lack of confounding with other demographic variables suggests its potential to explore cultural constructs as they relate to other behaviors, performance, or functioning.

In other cultural groups, acculturation has been examined increasingly as one of the factors accounting for variation in health behaviors. For example, acculturation has been found to be positively associated with ever having had a Pap test among young Asian-American women (Tang, Solomon, Yeh, Worden, 1999), having mammograms and clinical breast exams among Latinas (O'Malley, Kamer, Johnson, & Mandelblatt, 1999), illicit drug use among Mexican men and women (Vega, Alderete, Kolody, & Aguilar-Gaxiola, 1998) and greater alcohol consumption among Mexican American women (Alaniz, Treno, & Saltz, 1999). Among Korean Americans, high acculturation is related to higher body weight and lower physical activity (Lee, Sobal, & Frongillo, 2000). In addition, smoking behavior has been linked to acculturation. Chen, Unger, Cruz, and Johnson (1999) found greater smoking behavior and earlier onset of smoking among more highly acculturated Asian American youth, a relationship also documented in other Asian and Latino populations of varied ages (Ebin, et al., 2001; Lee, Sobal & Frongillo, 2000; and Unger et al., 2000).

Few studies have examined the relationship of acculturation and health behaviors among African-Americans (Landrine & Klonoff, 1994; Herd & Grube, 1996; Klonoff & Landrine, 1999; Brook, Whiteman, Balka, Win, & Gursen, 1997). Landrine and Klonoff (1996) used the AAAS to examine the role of acculturation in cigarette smoking and found that African Americans who scored as less acculturated were more likely to be smokers. Klonoff and Landrine (1999) later replicated this finding in a community sample. Here, the researchers found a significant association between the total acculturation score and smoking status, with less acculturated

African Americans being more likely to smoke. The role of acculturation in secondary prevention (e.g., breast cancer screening) has not previously been investigated.

Although breast self-exam (BSE) has not been proven unequivocally to be effective in detecting breast cancer or reducing mortality related to the disease, it has been recommended consistently by national clinical societies (e.g., American Cancer Society, American Society of Clinical Oncology) as an important aspect of breast cancer surveillance and has been shown to detect a substantial number of breast cancers (Porter, 1999). Among economically disadvantaged groups, cost can be a barrier to participating in clinical breast cancer screening (Rimer, 1992). Given that BSE is a cost-free screening procedure that is under a woman's personal control, examining BSE behavior among African American women is particularly relevant. Existing studies on BSE among African American women have yielded inconsistent results, with some indicating African American women tend to under-perform BSE (Underwood, 1999) and others indicating African American women tend to over-perform BSE (Epstein et al., 1997). While BSE under-performance is well recognized to decrease the utility of this screening modality, BSE over-performance may also decrease efficacy by reducing women's ability to detect gradual changes in the breast (Haagensen, 1952).

As an example of a self-initiated secondary prevention behavior, it is important to understand factors that may encourage or deter BSE among African American women. The aims of the present study were to re-examine the relationship of acculturation and smoking status in an urban, inner city sample of African American women, and to examine the role of acculturation in another health behavior (BSE frequency). The AAAS has been recently revised to drop 26 items (Klonoff & Landrine, 2000), based on feedback from other investigators who reported that

participants found many items objectionable. Thus, analyses reported here are for the revised scale.

METHOD

Participants.

African American women (N=66) attending an inner-city cancer-screening clinic completed study questionnaires. To be eligible, participants had to be 25 or older, able to read/write English, and able to provide meaningful informed consent. The study excluded women who had a personal history of neoplasm, or abnormal pathologic reports, or were pregnant.

A standard questionnaire (Valdimarsdottir et al., 1995) was used to obtain information on age, education, and other demographic variables. Age ranged between 26 -72 years (M = 45.00, SD = 10.70). Eighty-five percent completed at least some high school. Income was trichotomized into < $10,000 (18%); $10,000-$39,000 (61%); and > $39,000 (21%). Sixty-three percent were currently employed and 30% were currently married. Forty-five percent were "ever smokers," as indicated by their responses to a question taken from the National Health Interview Survey (Benson & Marano, 1995): "During your lifetime, have you smoked at least 100 cigarettes (5 packs)?" Smoking was unrelated to demographics in this data set.

Setting.

Data were gathered from women attending an urban cancer screening clinic, the Breast Examination Center of Harlem (BECH), who self-identified as African American. The BECH provides advanced, comprehensive diagnostic screening services to members of the Harlem

community. All services are provided at no out of pocket expense to the client. Ninety-seven percent of the BECH clientele, and 95% of the BECH staff were Black or Latina. Particularly relevant to this study, nurse practitioners at the BECH give clients instruction on how to properly perform BSE and frequency guidelines (i.e., once a month) are emphasized. Videotaped instructions on how to perform BSE also play repeatedly in the waiting area.

Procedure.

Participants were recruited from the BECH waiting room on scheduled clinic days by an African American female researcher (JG). After agreeing to participate, all were given an appointment to meet with the researcher three to four weeks afterwards to complete study questionnaires. This schedule was to ensure that subjects would receive results of cancer screening prior to the interviews. None of the women received abnormal results. One subject who required a follow-up clinic visit due to unclear or suspicious results was excluded from the study. All women completed standardized measures (described in detail below) that assessed African American acculturation and breast self-examination behavior in addition to the measures used in the larger study. As noted by the developers of the AAAS (Landrine & Klonoff, 1996) highly acculturated subjects may find the scale offensive, therefore, care was taken to explain the purpose of the measure to all participants. In our sample, only one woman refused to complete the measure, saying she did not see its relevance to her experience. Participants received $20 plus the cost of round trip public transportation for the visit.

Measures.

African American Acculturation Scale (AAAS). The original AAAS measure contained 74 items (Landrine & Klonoff, 1994) assessing eight dimensions of African American culture,

whereas the revised version (reported here) consists of 47 items (Klonoff & Landrine, 2000) assessing seven dimensions of African American culture. A subject's score on a sub-scale is computed as the sum of the answers on that sub-scale, and a Total Summary Score is also computed. A higher score is thought to represent more traditionally African American views.

Assessment of breast self-examination. Two questions based on published methods assessed breast self-examination frequency. First, participants were asked: "How often do you perform breast self-examination? (1) *More than once a month;* (2) *Once a month* (*12 times a year);* (3) *Every other month* (6 *times a year);* (4) *Four or five times a year*; (5) *Two or three times a year;* (6) *Once a year;* (7) *Never."* Under-performance was operationally defined as performing BSE less than once a month. Second, over-performance in the period following their clinical examination was evaluated with the question: "In the past three weeks, how many times did you perform breast self-examination? *(a) Never; (b) Once; (c)* 2-3 *times; (d)* 4-5 *times; (e) Six or more times."* Over-performance was operationally defined as performing BSE more than once during the prior three weeks. As would be expected, results on the two measures of BSE frequency were significantly related (chi-square F=55.36, $p < .001$).

RESULTS

Phase 1.

We first examined the psychometric properties and concurrent validity of the AAAS. Consistent with previously published results (Landrine & Klonoff, 1994), data from this sample (n=35) demonstrated a wide range of scores. Also consistent with published findings (Landrine

& Klonoff, 1994; Klonoff & Landrine, 1999), in this data set scores on the AAAS were not significantly related to demographic variables.

We next examined concurrent validity of the revised AAAS scales by following the previously published approach of the scale's developers. They argued that persons of an ethnic group who live in an ethnic-minority neighborhood are likely to be the more traditional members of their culture (because of constant exposure to the culture), whereas those who live in predominately White or integrated neighborhoods are likely to be more acculturated (Landrine & Klonoff, 1994). Thus, we examined the scores of the answers to the question, "I currently live in a Black neighborhood" and divided the subjects into two extreme groups: 1) the "Other residence" group consisted of the women in this sample who circled, "This is absolutely not true of me" (n = 5) and, 2) the "Black neighborhood residence" group who circled, "This is absolutely true of me" (n = 20). Analysis of the AAAS Total Summary Score revealed that the Black neighborhood group scored significantly ($F[1,23]=20.84$, $p < .0001$) higher (i.e., more traditionally African American) than the other residence group (i.e., more acculturated).

Next we examined the relationship between acculturation and smoking. These analyses revealed that ever smokers (n=16) scored higher than non-smokers (n=19) on the Total Summary Score ($F[1,34]=5.53$, $p < .05$). Descriptive statistics for the sub-scales suggested that the Family Practices and Interracial Attitudes sub-scales contributed to the group differences (see Table 1).

Finally, we examined the AAAS scores in relation to BSE frequency. ANOVA results revealed that the mean for BSE "Under-performers" (n = 17) differed from "Others" (n = 18) on the Total Summary Score. Women who under-performed BSE (i.e., less than once a month), scored lower (i.e., more acculturated). Consistent with these results, analysis of BSE over-

performance indicated that "Over-Performers" (n = 14) also differed from "Others" (n = 21) on the Total Summary Score (see Table 2).

Phase 2.

In this phase of the study, an additional 31 women completed only the Preference for African American Things sub-scale (12 items) in addition to the other study measures, to provide confirmatory data on the relationship between this sub-scale and BSE frequency. The focus on that sub-scale served to reduce participant burden, while providing additional data on the AAAS sub-scale that had the strongest significant relation to BSE frequency in Phase 1. Continuing to support results found in Phase 1 in the combined sample, women who under performed BSE in the combined sample (N = 66) scored significantly lower on the Preference for African American Things sub-scale ($F[1,65] = 6.42$, $p < .013$); the mean score for "Under-performers" (N = 31; mean 45.48, S.D. 13.82) versus "Others" (N = 35; mean 53.53, S.D. 11.98). For over-performance the pattern was also not altered from that seen in Phase 1; the mean Preference scores of "Over-Performers" (N = 23; mean 56.23 S.D. 9.42) was significantly higher than for "Others" (N = 43; mean 46.28, S.D. 14.01) ($F[1,65] = 9.29$, $p < .003$).

DISCUSSION

The objectives of this study were to re-confirm the psychometric properties and validity of the African American Acculturation Scale (AAAS) (Landrine & Klonoff, 1994) in an independent sample of urban, inner city African American women, to re-examine the relationship between acculturation and smoking status, and to investigate the role of acculturation in breast self-examination (BSE). We found ranges in variability for total acculturation and dimension

scores that were similar to those found by the scale's developers, and also found that women who lived in an African American community scored higher on the AAAS (i.e., less acculturated) compared to women who lived in an integrated community. Also consistent with initial reports by the scale's developers, we did not find responses on the AAAS to be associated with income or level of education. In addition, we found a relationship between acculturation and ever smoking, consistent with previous studies by the scale's developers (Landrine & Klonoff, 1996; Klonoff & Landrine, 1999). Supporting those studies, we found a negative association between acculturation and ever smoking, with less acculturated African American women more likely to report having been smokers at some point in their lives.

Interestingly, one acculturation dimension that the descriptive data suggested might be related to ever smoking in the present study, as well as those conducted by the scale's developers, was Family Structure and Practices. This dimension reflects the extent to which one's immediate and extended family adheres to practices, customs, and values specific to African American culture (Landrine & Klonoff, 1994). In this study, and in the studies by Landrine and Klonoff, smokers were more likely to score higher. The items contained in this sub-scale assess participation in traditional African American family practices (e.g., informal adoption or "child-keeping"). One hypothesis that may explain such findings is that individuals scoring higher on this sub-scale may be more likely to be exposed to extended family members who smoke, and therefore more likely to adopt the behavior themselves. Another acculturation dimension that the descriptive results suggested as potentially related to smoking was Interracial Attitudes. This dimension is designed to assess attitudes about Whites and White institutions, "cultural mistrust" (Landrine & Klonnof, 1996; Terrell & Terrell, 1981). One explanation for

these findings could be those individuals who have a great distrust of Whites or those who perceive greater racism (those scoring higher on the Interracial Attitudes dimension) may be more likely to smoke than those who do not (Landrine & Klonoff, 1996; Guthrie, Young, Williams, Boyd & Knitner, 2002).

The final aim of this study was to explore the role of acculturation in BSE under-performance and over-performance. Breast self-exam is related to earlier pathological stage of cancer diagnosis and symptom presentation, and continues to be recommended as an important breast cancer screening modality by the American Cancer Society (ACS, 2004) and the American Society of Clinical Oncology (Smith et al., 1999). With regard to rates of BSE performance in general, fifty-one percent of the women in this study reported performing BSE at least once a month. This rate is consistent with the rate (49.7%) reported in a random sample of low income, African American women ages 40 and over living in a Florida city (Mickey, Durski, Worden, & Danigelis, 1995) and also falls into the range (41% to 67%) reported for other populations of women 50 and older in the U.S. (NCI Breast Cancer Screening Consortium, 1990).

While under-performing BSE has obvious implications for the utility of this screening modality, less appreciated are the potential drawbacks to over-performing BSE. It has long been recognized that over-performing BSE may decrease a woman's ability to detect gradual changes in the breast, as well as induce cancer anxiety (Haagensen, 1952). Excessive BSE performance may also be associated with increased numbers of false positive findings, which also may result in increased anxiety (Lerman, Kash, & Stefanek, 1994; Haefner, Becker, & Janz, 1989). Women may also use their over-reliance on BSE as a screening modality as a reason for opting out of, or

not adhering to, other screening modalities such as mammography (Epstein & Lerman, 1997). Both under- and over-performance of BSE may then lead to diminished utility of this screening modality.

Results of the present study revealed significant associations between acculturation and BSE frequency. Women whose responses indicated that they generally under-perform BSE were more acculturated. BSE over-performers, as based on the respondent's most recent reported behavior (past three weeks), were less acculturated. Interestingly, one acculturation dimension that the descriptive data suggested might be related to BSE was the Preference for African American Things subscale. This subscale reflects the extent to which an individual has a preference for African American newspapers, periodicals, music, activities, arts, and people (Landrine & Klonoff, 1994), and is similar to other conceptualizations of acculturation (Snowden & Hines, 1994).

Considered together, these findings suggest the importance of identifying specific mechanisms that may influence the behavior of interest. Different health behaviors are likely to be associated with different cultural dimensions. For example, Tang et al. (1999) found that among Asian American women, modesty was related to BSE, but not other aspects of culture. And, the present study suggested that the Family Structure and Practice dimension may be particularly important with regard to lifetime smoking status, consistent with Landrine and Klonoff (1996) and Klonoff and Landrine (1998). Future research should begin to investigate cultural thought and behaviors that are thought to represent a more traditional African worldview, such as a holistic and communal orientation, extended self identity and spirituality (e.g., see Montgomery, Fine and Myers, 1990; Oshodi, 1999; Baldwin, 1984). In addition, more

politically informed values such as Africentrism (Grills & Lonshore, 1996) should be considered. Such research may thus assist us in targeting specific barriers for intervention.

In this sample traditional African American women were more likely to smoke (a negative effect on health behavior), and more likely to over-perform BSE (potentially, also a negative effect on health behavior), and acculturated African Americans were less likely to smoke (a positive effect on health) and more likely to under-perform BSE (a negative effect on health). While the literature has demonstrated that acculturation has different effect on different health behaviors for the same ethnic group (Crespo, et al., 2001; Gardner, et al., 1995; Otero-Sabogal, et al., 1995), conflicting results may be due to a response bias or extreme response style, as has been found among Hispanics (Cheung, et al., 2000; Marin, et al., 1992; Watkins and Cheung, 1995). In this sample of African American women, it may be that the less traditional group are those more likely to be the "yeah-sayers," scoring high on both smoking and BSE. However, an alternative hypothesis may be that one's level of acculturation may shape the way information relating to health is interpreted. For example, Klonoff and Landrine (1999) found that black females who agreed that AIDS is a conspiracy against them tended to be more culturally traditional. The same idea may hold in these current findings such that traditional black women in this study who were over performing BSE may not believe that once a month as prescribed by the government is enough. Reconciling the fact that traditional black women are more likely to smoke may be less related to government guidelines regarding smoking, and more related to the stress related to their experiencing significantly greater discrimination than acculturated counterparts (Klonoff and Landrine, 1999; Landrine and Klonoff, 1996), exposure to family members that also smoke (as demonstrated by the relationship of smoking to the family

attitudes and interracial attitudes subscales, and the targeting of African Americans by the tobacco industry, especially the tobacco industry's strategy of targeting magazines tailored to African Americans (Balbach, Gasior, and Barbeau, 2003). Our finding that those who are less acculturated are more likely to be smokers is consistent with the tobacco industry's special efforts to target African Americans since the early 1960's (Weinbrenner, 2001).

Limitations to this study should be noted. Because the sample size was relatively small and women were recruited specifically from a low-income, inner city breast cancer-screening center, our results cannot be generalized to all African American women. Moreover, it is likely that the prevalence of BSE under-performance and/or over-performance may be higher among women who do not receive BSE education and training as those in our sample did. We deliberately selected women who were instructed by African American health care providers in proper BSE technique in order to hold BSE training, knowledge of BSE guidelines, and ethnic background of health care providers constant.

Taken together, our findings highlight the importance of identifying specific acculturation mechanisms that may influence health behaviors of interest. Different health behaviors may be selectively influenced by different acculturation dimensions. Clearly, the value of the concept of acculturation in clinical research depends on how it is operationalized and utilized in understanding and predicting the spectrum of health behaviors related to the risk of disease. By identifying specific acculturation components that facilitate or deter health behaviors, we may be better able to implement interventions to improve health status among different ethnic and cultural communities.

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Table 1.
Relationship between AAAS scores and history of smoking

	Ever Smoked (n=16) Mean (S.D.)	Non Smokers (n=19) Mean (S. D.)	F	Sig.
Total Summary Score	282.56 (38.12)	241.42 (60.52)	5.53	.025
Subscales	**OR (95% C.I.)**			
Preferences	1.05 (0.99 – 1.11)			
Family Practices	1.09 (1.00 – 1.20)			
Health Beliefs	1.03 (0.94 – 1.12)			
Socialization	1.01 (0.94 – 1.07)			
Religion	1.07 (0.98 – 1.17)			
Interracial Attitudes	1.07 (1.00 – 1.14)			
Superstitions	1.10 (0.99 – 1.21)			

Table 2.
Relationship between AAAS scores and compliance with breast self exam frequency recommendations

	Under Performance Assessment — Past Year				Over Performance Assessment — Past Three Weeks			
	Under Performers (n=17)	Others (n=18)			Over Performers (n= 14)	Others (n= 21)		
	Mean (S.D.)	Mean (S.D.)	F	Sig.	Mean (S.D.)	Mean (S.D.)	F	Sig.
Total Summary Score	237.76 (59.81)	281.44 (40.95)	6.42	.016	289.57 (33.86)	240.67 (58.07)	8.05	.008
Subscales	**OR (95% C.I.)**				**OR (95% C.I.)**			
Preferences	1.10 (1.02 – 1.19)				1.15 (1.03 – 1.28)			
Family Practices	1.04 (0.97 – 1.13)				1.04 (0.96 – 1.13)			
Health Beliefs	1.05 (0.96 – 1.15)				1.03 (0.94 – 1.12)			
Socialization	1.05 (0.98 – 1.12)				1.08 (0.99 – 1.17)			
Religion	1.08 (0.99 – 1.18)				1.11 (0.99 – 1.24)			
Interracial Attitudes	1.02 (0.96 – 1.08)				1.02 (0.96 – 1.08)			
Superstitions	1.08 (0.98 – 1.19)				1.10 (0.99 – 1.23)			

Note: Re-analyses excluding women whose responses revealed long-term under performance and short-term over performance (n=4) yielded an identical pattern of results.

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Family Histories of Breast Cancer, Coping Styles, and Psychological Adjustment[1]

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Although women with family histories of breast cancer (FHBC+) have been reported to have higher levels of cancer-specific and general distress than have women without such histories (FHBC−), there has been considerable variability in levels of distress found. This study examined individual differences in the use of coping strategies as likely moderators of the relationship between FHBC and psychological outcomes. One hundred and sixteen healthy women (47 FHBC+ and 69 FHBC−) participated. Results revealed that passive coping style was associated with higher levels of cancer-specific distress among FHBC+, but not among FHBC−. This interaction was not found for negative or positive affect. The passive coping style was associated with higher levels of negative affect across both groups. These results suggest that passive coping has negative implications for FHBC+ women and imply that individualized coping training programs targeting this coping strategy may prove useful for these women.

KEY WORDS: family histories of breast cancer; coping; psychological distress; positive affect.

Breast cancer is the second most common cancer and the second leading cause of cancer death among American women (American Cancer Society, 2003). It is estimated that in 2003, approximately 211,300 women in the United States would be diagnosed with breast cancer and approximately

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39,800 died of breast cancer (American Cancer Society, 2003). The lifetime risk of breast cancer for women without family histories of breast cancer (FHBC) in the United States is 1 in 8 (American Cancer Society, 2003). The risk becomes even higher for women if they have family histories of the disease. For example, women with a single first-degree relative affected with breast cancer are two to three times more likely to develop breast cancer than women without an affected first-degree relative (Claus *et al.*, 1998; Offit and Brown, 1994; Slattery and Kerber, 1993).

Substantial evidence indicates that the experience of breast cancer in a first-degree relative is a life stressor for women particularly for those with family histories of the disease (see for a review Bovbjerg and Valdimarsdottir, 2001). Healthy women with FHBC have been found to have higher levels of cancer-specific distress than women without such histories (Lloyd *et al.*, 1996; Valdimarsdottir *et al.*, 1995; Zakowski *et al.*, 1997). Surveys of women with FHBC have consistently revealed high levels of cancer-specific distress. For example, Lerman *et al.* (1993) found that 53% of their sample of first-degree relatives of patients with breast cancer experienced intrusive thoughts about breast cancer, with 30% of these women indicating that their breast cancer worries interfered with their daily lives. More recently, Neise *et al.* (2001) found that nearly a third of their sample of women with family histories of breast cancer experienced intense cancer-specific psychological strain.

Higher levels of general distress have also been observed among women with FHBC (Audrain *et al.*, 1998; Baider *et al.*, 1999; Gilbar, 1997, 1998; Kash *et al.*, 1992; Lerman *et al.*, 1993; Lloyd *et al.*, 1996; Valdimarsdottir *et al.*, 1995; Wellisch *et al.*, 1991). Kash *et al.* (1992) found that 27% of women with FHBC reported levels of distress that were at least 1 standard deviation above standardized population means on the Brief Symptom Index (BSI; Derogatis 1993). However, other studies have found that having a family history of breast cancer is not significantly associated with elevated levels of general distress (e.g., Lloyd *et al.*, 1996; Wellisch *et al.*, 1991; Zakowski *et al.*, 1997).

The findings from the above studies suggested that not all women with FHBC report higher levels of both cancer-specific and general distress, underscoring the need to examine factors that may account for individual differences in distress levels. The coping literature has compellingly established that individuals' coping strategies moderate the impact of a variety of stressors on psychological distress (Folkman and Moskowitz, 2000a; for reviews, see Lazarus, 2000; Lazarus and Folkman, 1984), but little attention has been paid to the role of coping among women who have experienced cancer in their families.

Coping strategies have been grouped according to the expected outcome: active and passive coping (Brown and Nicassio, 1987). Active coping strategies have been defined as those strategies utilized to deal with stress by using the individual's internal resources, whereas passive coping strategies have been defined as those strategies utilized to deal with stress by using the individual's external resources (Brown and Nicassio, 1987). Numerous studies, using various coping measures, have reported that active coping strategies are associated with better psychological adjustment, such as lower emotional distress, among both patients (Epping-Jordan *et al.*, 1999; Snow-Turek *et al.*, 1996; Stanton *et al.*, 2000) and healthy individuals (Leslie *et al.*, 2002; McMahon and Watts, 2002; Musil and Ahmad, 2002). On the other hand, passive coping strategies have been associated with maladaptive outcome measures, such as increased depression and distress among patients (Ben-Zur *et al.*, 2001; Manne *et al.*, 1994; Osowiecki and Compas, 1999) and healthy individuals (Holmes and Stevenson, 1990; Mercado *et al.*, 2000; Snow *et al.*, 1996; Updegraff and Taylor, 2000). Recent studies have also shown that coping, in particular active coping, is associated not only with lower psychological distress but also with higher levels of positive affect (Folkman and Moskowitz, 2000a,b).

A number of studies have demonstrated that individuals use similar coping strategies to cope with various stressors. For example, studies of college students (Amirkhan *et al.*, 1995) and spouse caregivers of patients with Alzheimer's disease (Hooker *et al.*, 1994) revealed that these participants consistently used help seeking to cope with various naturally occurring stressors. Supporting a dispositional conceptualization of coping (Costa *et al.*, 1996), findings from recent studies have also shown that coping styles are associated with personality characteristics, in particular neuroticism and extroversion (Sørlie and Sexton, 2001a; Watson and Hubbard, 1996).

To date, only one study (Wellisch *et al.*, 1991) has compared women with FHBC to women without such family histories to explore differences in utilization of dispositional coping strategies. Using the Ways of Coping Questionnaire (WCQ), Wellisch *et al.* (1991) found that women with FHBC were quite similar in their use of particular coping strategies compared to women without such family histories. However, this study did not examine the relation between coping and psychological distress (e.g., cancer-specific or general distress) or positive affect. In addition, this study did not investigate if the relations between an individual's status of family history of breast cancer and psychological adjustment differ by the individual's coping styles.

Thus, this study was designed to replicate and extend Wellisch and colleagues' study by examining whether coping styles play a different role in the levels of an individual's psychological distress or positive affect, depending on the individual's status of family history of breast cancer. On the basis of

the literature reviewed above, we hypothesized that (a) women with and without FHBC would use coping strategies in a similar degree; (b) passive coping style would be associated with higher levels of cancer-specific distress and general negative affect, which would be stronger for women with FHBC than for women without such histories; and (c) active coping style would be associated with lower levels of cancer-specific distress and negative affect, which would be stronger for women with FHBC than for women without such histories. Lastly, in light of recent findings that coping is associated with positive affect, we explored whether active coping style was differentially associated with positive affect depending on the women's FHBC status.

METHOD

Participants

One hundred and sixteen women, with first-degree relatives with breast cancer ($N = 47$) and without such relatives ($N = 69$), were included in this study, which is part of a larger longitudinal investigation of women with FHBC (Erblich *et al.*, 2000). Participants were recruited by advertisements placed in three medical centers in New York City. Less than 10% of contacted women declined to participate. Consistent with IRB requirements at our institution, no data is available on these women. The mean age of the sample was 43 years (range = 25–69; SD = 10.6). Most participants were ethnic minorities (77% African American, 10% Hispanic, 1% Asian). Over a third of the participants had completed college and a third of the participants were married. Among women with FHBC, average time since the diagnosis of breast cancer of the first-degree relatives was 23 years (range = 3–54 years; SD = 12.9).[5]

Procedures

Participants provided written informed consent prior to participating in this study. Questionnaires were completed in the presence of an investigator who was available to clarify any items. To reduce burden at study assessment visits, participants were permitted to complete the demographic portion of the questionnaire and the coping measure at home and return it later. Questionnaire assessments of psychological outcome data were obtained on three

[5]The zero-order correlations between the length of time since diagnosis of cancer in first-degree relatives and our outcome measures (cancer-specific distress, negative affect, and positive affect) were not significant ($-0.29 < r < .12$, $ps > 0.18$).

separate occasions approximately 1 month apart to examine stability of psychological outcome variables. As no main effects or interaction effects with assessment time were significant, each measure was averaged across the three assessments to provide a more reliable measure of these constructs. The average scores were then used in the analyses.

Measures

Demographics

Participants completed standard questions assessing demographics, including age, education, ethnicity, and income.

Family Histories of Breast Cancer

Participants completed a standardized questionnaire assessing family histories of cancer (Erblich *et al.*, 2000). The questionnaire included items asking whether or not the participant's first-degree relatives (e.g., mother, sister, or daughter) has been diagnosed with breast cancer. Among women who had first-degree relatives with breast cancer, four women had two relatives, one woman had three relatives, and the rest of women had one relative with breast cancer. In addition, participants reported how likely they believed they were to develop breast cancer sometime during their lives, on a scale ranging from 0% (not at all likely) to 100% (extremely likely) (Durfy *et al.*, 1999; Valdimarsdottir *et al.*, 1995; Zakowski *et al.*, 1997).

Coping Styles

Participants indicated the extent to which they used different coping strategies in response to stressful events, using WCQ (Folkman and Lazarus, 1988), in a 4-point Likert-style format (0 = not used, 3 = used a great deal). To reduce participant burden, 31 items from eight subscales (3–4 items per subscale), which had high factor loadings (Folkman *et al.*, 1986), were included in the present study.

Because of instability in factor structure of WCQ, researchers have conducted factor analyses for their own samples to determine types of coping strategies (e.g., Edwards and O'Neil, 1998; Sørlie and Sexton, 2001b; Tennen and Herzberger, 1985). Thus, we also conducted factor analysis for the data in our sample. Factor analysis with varimax rotation and with examining the scree plots of eigenvalues (Cattell and Vogelmann, 1977) extracted

nine factors that have eigenvalues greater than 1 (Kaiser, 1960) (65.2% of the variance was explained). All factor loadings of each item for the corresponding primary factory were greater than or equal to 0.40. Second-order factor analysis with nine factor scores using varimax rotation extracted two higher-order factors (44% of the variance was explained). The first higher-order factor (eigenvalue = 2.07) includes 16 items indicating acceptance or denial of stressors (see Table I), which was labeled *passive coping*. The second higher-order factor (eigenvalue = 1.89) includes 15 items indicating effortful seeking to manage or alter the problem, which was labeled *active coping*.[6] Composite scores for each of these two coping strategies were created by averaging relevant items and used in the subsequent analyses as measures of individual differences in coping styles. Both coping style composites had good internal consistency ($\alpha = 0.80, 0.79$ for passive and active coping, respectively).

Neuroticism and Extraversion

To examine whether the effects of dispositional coping styles in this study would be independent of those of personality traits, two related personality characteristics, neuroticism and extraversion, were included in a set of analyses as covariates (see "Moderating Effects of Coping Styles" sections under Results). Neuroticism and extraversion were measured using the corresponding 12-item subscales of the NEO-FFI (Costa and McCrae, 1992), using a 5-point Likert response format (1 = strongly disagree, and 5 = strongly agree). Individuals high in neuroticism are characterized as worrying, nervous, emotional, insecure, inadequate, and hypochondriacal (McCrae and Costa, 1997). Individuals high in extraversion are characterized as joyful, energetic, and dominant (McCrae and Costa, 1997). Neuroticism

[6]The loadings on other factors which were not reported in Table I were all less than or equal to 0.40, except the following six items. The factor loading of the item "I made a promise to myself that things would be different next time" for the first-order factor 1 was 0.65, while the factor loading for the first-order factor 4 was 0.41. The factor loading of the item "Talked to someone who could do something concrete about the problem" for the first-order factor 3 was 0.56, while the factor loading for the first-order factor 1 was 0.44. These cross-loading problems of these two items disappeared by a subsequent factor analysis with oblique rotation. On the other hand, the cross-loadings remained significant for the rest four items: "Stood my ground and fought for what I wanted" for the first-order factor 1 was 0.56 and for the first-order factor 5 was 0.50 (0.49 with oblique rotation); "I let my feelings out somehow" for the first-order factor 7 was 0.73 and for the first-order factor 5 was 0.42 (0.41 with oblique rotation); "I tried not to act too hastily or follow my first hunch" for the first-order factor 8 was 0.75 and for the first-order factor 4 was 0.49 (0.47 with oblique rotation); "I apologized or did something to make up" for the first-order factor 9 was 0.64 and for the first-order factor 5 was 0.43 (0.42 with oblique rotation). Overall, the factor structure of WCQ in this study did not have complex loadings cross factors.

Table I. Factor Analyses on 31-Item Ways of Coping Questionnaire

	First-order factor loadings	Second-order factor loadings	
		Passive	Active
Factor 1		0.41	**0.67**
I knew what had to be done, so I doubled my efforts to make things work	0.73		
I changed something so things would turn out all right	0.70		
I made a plan of action and followed it	0.67		
I made a promise to myself that things would be different next time	0.65		
Stood my ground and fought for what I wanted	0.56		
Tried not to burn my bridges, but leave things open somewhat	0.43		
Factor 2		**0.71**	−0.07
I tried to keep my feelings to myself	0.75		
Didn't let it get to me; refused to think too much about it	0.75		
Tried to forget the whole thing	0.70		
Made light of the situation; refuse to get too serious about it	0.60		
I kept others from knowing how bad things were	0.59		
Went on as if nothing had happened	0.59		
Factor 3		0.17	**0.65**
I asked a relative or friend I respected for advice	0.89		
I talked to someone about how I was feeling	0.77		
Talked to someone to find out more about the situation	0.68		
Talked to someone who could do something concrete about the problem	0.56		
Accepted sympathy and understanding from someone	0.44		
Factor 4		**0.69**	0.07
Had fantasies or wishes about how things might turn out	0.84		
Wished that the situation would go away or somehow be over with	0.67		
Criticized or lectured myself	0.54		
Tried to make myself feel better by eating, drinking, smoking, using drugs or medication, or that sort of thing	0.51		
I avoided being with people in general	0.50		

Table I. (*Continued*)

	First-order factor loadings	Second-order factor loadings	
		Passive	Active
Factor 5		0.07	**0.59**
Tried to get the person responsible to change his or her mind	0.83		
I expressed anger to the person(s) who caused the problem	0.68		
Factor 6		**0.52**	0.34
Found new faith	0.77		
I prayed	0.74		
I rediscovered what is important in life	0.63		
Factor 7		−0.23	**0.70**
I let my feelings out somehow	0.73		
Just concentrated on what you had to do next—the next step	0.71		
Factor 8		**0.57**	0.00
I tried not to act too hastily or follow my first hunch	0.75		
Factor 9		**0.49**	0.25
I apologized or did something to make up	0.64		

and extraversion measures had reasonable internal consistency in the present study ($\alpha = 0.82, 0.58$, respectively).

Breast-Cancer-Specific Distress

Breast-cancer-specific distress was measured using the 15-item Impact of Event Scale (IES; Horowitz *et al.*, 1979), replacing "event" with "breast cancer." Responses on the scale were for the past three weeks, using a 4-point Likert-style scale (0 = not at all, 1 = rarely, 3 = sometimes, and 5 = often). The IES has two subscales: Intrusion, which assesses intrusive thoughts and feelings (seven items), and Avoidance, which assesses avoidance of certain thoughts, feelings, or situations (eight items). Both subscales (Erblich *et al.*, 2000; Kash *et al.*, 1992; Lerman *et al.*, 1993; Valdimarsdottir *et al.*, 1995; Zakowski *et al.*, 1997) and the total composite score (IES; Schwartz *et al.*, 1995) have been widely used to assess the level of cancer-specific distress among individuals with family histories of cancer. In the present study, the two subscales were highly and significantly correlated ($r = 0.80$, $p < 0.001$) and were therefore summed to make a total composite score on IES (Schwartz *et al.*, 1995). The IES measure had good internal consistency ($\alpha = 0.91$).

Negative Affect and Positive Affect

Negative affect and positive affect were assessed using a Negative Affect (seven items) and Positive Affect (seven items) Scale (NAPAS) derived from the Profile of Mood States (Guadagnoli and Mor, 1989; Valdimarsdottir and Bovbjerg, 1997). Participants rated the items for the day of assessment using a 5-point Likert-style scale (0 = not at all, 4 = extremely). Negative affect and positive affect scores of the NAPAS had good internal consistency in the present study (α = 0.94, 0.89, for negative affect and positive affect, respectively).

RESULTS

Before testing the primary study question, possible differences in demographic variables between the women with FHBC (FHBC+) and those without (FHBC−) were examined for possible inclusion in study analyses as covariates. There were no group differences in age (M = 44.41 years for FHBC+, 41.48 for FHBC−), education (85% completed high school for FHBC+, 88% for FHBC−), or proportion of African American participants (77% for FHBC+, 74% for FHBC−). There was a trend for a group difference in income (70% FHBC+ had an income of greater than $20,000, 54% for FHBC−, $\chi^2 = 3.22$, $p < 0.06$) and there was a significant group difference in the level of perceived risk of developing breast cancer (49.57% for FHBC+, 37.0% for FHBC−, $t = 2.53$, $p < 0.05$). Therefore, income and perceived risk were included as covariates in subsequent analyses. Because there was a substantial number of ethnic minorities in the study sample, ethnicity was also included as a covariate.[7]

Zero-order correlational analyses were also conduced to examine the relation among the main study variables (Table II). Higher levels of passive coping were associated with higher level of distress (cancer-specific distress and negative affect), whereas higher levels of active coping were associated with higher levels of positive affect. In addition, the two personality measures were related to both the coping measures and the psychological outcome measures. Therefore, the two personality characteristics were included in the last set of subsequent regression analyses to determine coping variables' contribution to each psychological correlate, relative to personality variables.

[7]We included "ethnicity" as a main study variable to examine the main effects of ethnicity as well as interaction effects with other study variables. We did not find any significant main or interaction effects.

Table II. Correlation Coefficients Among Coping Styles, Neuroticism, Extraversion, Psychological Distress, and Positive Affect

	1	2	3	4	5	6
1. Passive coping	—					
2. Active coping	0.35***	—				
3. Neuroticism	0.38***	0.03	—			
4. Extraversion	−0.19*	0.10	−0.22*	—		
5. IES	0.29***	0.14	0.30***	−0.25**	—	
6. Negative affect	0.42***	0.12	0.39***	−0.30***	0.23*	—
7. Positive affect	0.07	0.22*	−0.15	0.35***	0.00	−0.20*

Note. IES = total composite score of Impact of Event Scale.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Family History Group Differences in Coping Styles

Univariate analyses to test group differences in coping styles with Bonferroni corrections for multiple significant tests (Rosenthal and Rosenow, 1991) revealed that women in the FHBC+ group ($M = 1.14$, $SD = 0.51$) utilized the active coping strategies less frequently than women in the FHBC− group ($M = 1.41, SD = 0.50$), $t(114) = 2.93$, $p < 0.05$. More specifically, women having FHBC less frequently used planful problem-solving confronting (Factor 1), than did women without FHBC, $t(114) = 2.94$, $p < 0.05$.

Moderating Effects of Coping Styles

Two sets of hierarchical regression analyses were conducted on each outcome measure to examine the main effects of study variables and the hypothesized moderating effects of coping in the relationship between having FHBC and psychological correlates. The first set of analyses tested main study hypotheses regarding the effects of the FHBC and coping styles. The second set of analyses was supplementary to examine if the findings in the first set of analyses remained after the effects of neuroticism and extraversion were included.

In the first set of hierarchical regression analyses, the three covariates (i.e., ethnicity, income, and perceived risk) were entered in the first step. A dummy coding for family history group (1 for women with FHBC; 0 for women without FHBC) and the two coping style scores (i.e., passive and active) were entered in the second step to examine the main effects of these variables. In the third step, interaction terms (two- and three-way) were entered into the equation (Table III).

Table III. Hierarchical Regression on Breast-Cancer-Specific Distress (IES), Negative Affect, and Positive Affect

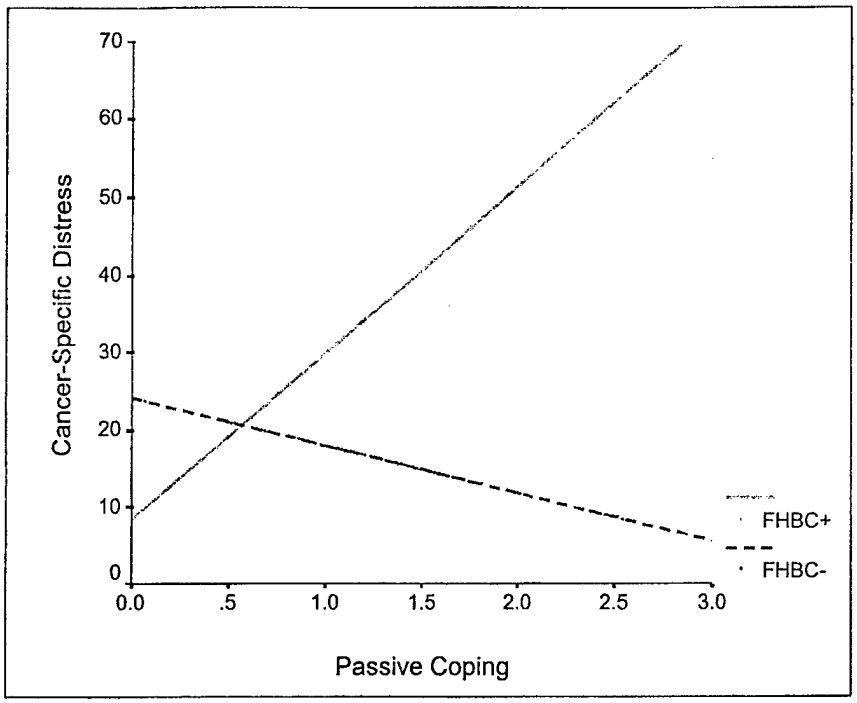
	IES		Negative affect		Positive affect	
	ΔR^2	β	ΔR^2	β	ΔR^2	β
Step 1: Covariates	0.12**		0.11**		0.05	
Ethnicity		0.10		−0.09		0.21*
Income		−0.19*		−0.35***		−0.02
Perceived risk		0.27**		0.10		0.02
Step 2: Main effects	0.09**		0.14***		0.07*	
Family histories of breast cancer (FHBC)		0.19*		−0.05		0.14
Passive coping (Pass)		0.29**		0.40***		−0.01
Active coping (Act)		0.05		−0.03		0.25**
Step 3: Interaction effects	0.04		0.02		0.02	
FHBC × Pass		1.43*		−0.56		0.40
FHBC × Act		0.54		−0.13		0.68
Pass × Act		0.55		−0.30		0.68
FHBC × Pass × Act		−1.16		0.18		−0.37

Note. Ethnicity: 0 for Non-African American, 1 for African American; Income: 0 for ≤20K, 1 for >20 K; Family History (FHBC), 0 for women without family histories of breast cancer, 1 for women with family histories of breast cancer; IES = total composite score of Impact of Event Scale.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

As shown in the first column of Table III, the main effects of FHBC group and passive coping style on breast-cancer-specific distress were significant. The FHBC+ women and women who utilized passive coping strategies were more likely to report higher levels of breast-cancer-specific distress. The hypothesized two-way interaction effect between family history group and passive coping was significant. The source of this interaction was determined with follow-up regression analyses, which revealed a significant positive association between passive coping and breast-cancer-specific distress for the FHBC+ group ($\beta = 0.83$, $p < 0.05$), but not for the FHBC− group ($\beta = -0.04$, *ns*) (Figure 1). No other main or interaction effects were significant.

The results with respect to negative affect are shown in the second column of Table III. The main effect of passive coping was significant. Use of a passive coping style was related to a higher level of general negative affect. The hypothesized interaction effect between family history group and passive coping was not significant. No other main or interaction effects were significant.

Finally, the results with respect to positive affect are shown in the third column of Table III. The main effect of active coping was significant. Use of an active coping style was related to a higher level of positive affect. The hypothesized interaction effect between family history group and



Note: FHBC+ : Women with family histories of breast cancer;
FHBC- : Women without family histories of breast cancer

Fig. 1. Interaction effect of FHBC and passive coping on cancer-specific distress.

active coping was not significant. No other main or interaction effects were significant.

In the second set of hierarchical regression analyses, neuroticism and extraversion scores were added in the second step of the same hierarchical regression equation that was used above. Two- and three-way interactions among family history group, neuroticism, and extraversion were added in the third step. Results revealed that the significant main and interaction effects found in the first set of analyses remained significant, except for the main effect of passive coping on cancer-specific distress which became nonsignificant ($\beta = 0.18, ns$). The results from this second set of hierarchical regression analyses, including personality characteristics as study variables, indicated

that the main effects of coping styles on general affect and the moderating effect of passive coping on breast-cancer-specific distress among women with FHBC were all independent of effects of personality characteristics.

DISCUSSION

The main findings of this study were that women with FHBC used coping strategies in differing degree, compared with women without such histories, and the use of passive coping strategies was adversely related to cancer-specific distress among women with FHBC, while that was not the case among women without FHBC.

Differences in Utilization of Coping Styles Between Women With FHBC and Women Without Such Histories

The findings in this study showed that women who have a first-degree relative with breast cancer were less likely to report using active coping strategies than were women without having such a relative. These findings are not consistent with Wellisch and colleagues' findings that there were no group differences in utilization of coping strategies for healthy adult daughters of women with breast cancer compared to those whose mothers did not have breast cancer (Wellisch *et al.*, 1991). The explanation for these discrepant results is not clear. One possibility is ethnic differences between the two study samples. The participants in Wellisch and colleagues' study were all Caucasian, while the sample in this study was primarily made up of ethnic minorities. Differences in coping with stress by different ethnic groups among young adult community samples have been found (e.g., Bjorck *et al.*, 2001). Further investigations are needed to better understand the factors that may account for reduced use of coping strategies among women with FHBC.

Moderating Effects of Utilization of Coping Styles

The second and third research hypotheses focused on family history group differences in the associations between coping styles and psychological adjustment. The study hypotheses were that the coping styles would play a different role in levels of an individual's psychological distress, depending on the individual's status of FHBC. Use of passive coping style was hypothesized to be associated with higher levels of cancer-specific distress and general negative affect, which would be more prominent among women with

FHBC than among women without such histories. Findings in the present study supported the hypothesis for a moderating effect of coping (Ensel and Lin, 1991; Lazarus, 2000) on cancer-specific distress. Specifically, passive coping style was associated with a higher level of cancer-specific distress among healthy women with FHBC, while this pattern was not found among women without such family histories. The findings of the present study suggest that the greater use of passive strategies to cope with stressors, such as self-controlling, avoidance, and distancing, may aggravate the degree to which individuals who have experienced breast cancer in their close family members have intrusive thoughts and feelings about breast cancer. This finding is particularly important because women with FHBC often have higher levels of cancer-specific distress. The findings in this study contribute to coping literature by expanding the scope of coping research to a population of healthy women who had experienced breast cancer in their first-degree relatives.

The relationship between passive coping and negative affect, unlike cancer-specific distress, did not differ between the two family history groups. Rather, greater use of passive coping was associated with higher levels of negative affect across both groups, which is consistent with a plethora of studies in coping literature (see Lazarus, 2000). These results support the notion that although coping is an initial effort to minimize the negative impact of stress, the consequences of utilizing certain coping strategies may not always meet this purpose (see Neufeld, 1999; Updegraff and Taylor, 2000). However, future studies should replicate the present findings with regard to the different effects of passive coping on the relationship between having family history of breast cancer and either cancer-specific distress or general negative affect.

Another hypothesis in this study was that active coping style would be associated with lower levels of cancer-specific distress and negative affect. Contrary to our hypothesis, active coping style was not significantly related to either cancer-specific distress or negative affect. There was a high degree of colinearity between the active and passive coping styles ($r = 0.35$), which might result in the null findings for active coping in the regression analyses for the cancer-specific distress and negative affect. Active coping style, however, was significantly associated with a higher level of positive affect in this study, findings which are consistent with existing studies (Billings *et al.*, 2000; Folkman *et al.*, 1994; Moskowitz *et al.*, 1996; Snow-Turek *et al.*, 1996). This association between active coping and positive affect was found for both family history groups. This finding supports an emerging view that use of active coping may be particularly predictive of positive affect (Folkman and Moskowitz, 2000a,b). Findings in the present study suggest that individuals regardless of their FHBC may benefit from using active strategies to

cope with stressors, such as seeking social support and planning for solving problems, to enhance their positive affect.

The findings in this study also revealed a unique contribution of dispositional coping styles above and beyond that of the well-established traits of neuroticism and extraversion in accounting for variability in healthy women's psychological adjustment to having experienced breast cancer in their first-degree relatives. Together these findings suggest women with FHBC may benefit from intervention programs designed to help them minimize their use of passive coping strategies.

Limitations and Directions for Future Studies

It has been suggested that the relationship between coping and affect may be reciprocal (Lazarus, 2000). For example, utilization of certain coping strategies, such as passive coping, may lead to more distress in the presence of stressor, or alternatively, distressed individuals may be more likely to engage in such coping strategy. Participants voluntarily responded to advertisements placed in three medical centers to participate in the study, so we cannot also rule out a selection bias. Prospective longitudinal studies and randomized theory-based intervention studies are needed to determine the directionality of putative causal relationships between coping and affect (Lazarus, 2000).

Generalizability of the current findings to samples with fewer ethnic minority participants needs to be confirmed. Although we found no significant ethnic group differences in makeup of our FHBC groups, additional studies with diverse ethnic samples with large number of ethnic minority are needed to examine the role of ethnicity in women's response to having family histories of breast cancer.

An individual's coping strategy can be modified for different situations, when dealing with different type of stressors, or depending on perceived controllability over outcomes (e.g., Schwartz *et al.*, 1999). Thus, an individual's coping strategy to deal with the stressor of having a history of breast cancer in the family may be different from what they use to deal with other stressors. Future studies that assess coping strategies specifically used by these women for dealing with their FHBC may help to further elucidate the role of coping in adjustment to this stressor.

The associations between either passive coping or neuroticism and either IES or negative affect, and between active coping or extraversion and positive affect might be exaggerated because of shared domain variance and similar items embedded in each measure. For further clarification of these associations, it would be beneficial to include non-self-report measures, such

as behavioral observation, physiological data, or ratings of the participants' psychological functioning by close family members or friends.

In addition, woman with multiple relatives with breast cancer might be expected to exhibit more distress than a woman with a single relative with breast cancer. We ran Pearson correlation analyses between the number of relatives with breast cancer and three psychological outcomes in this study. The r ranged from 0.01 to 0.13 ($0.39 < p < 0.96$). This question, however, needs to be tested with a larger sample of women with various numbers of relatives with breast cancer.

Finally, the study sample was relatively small. Thus, statistical power might be limited, which may be related to the null findings.

CONCLUSION

To our knowledge, this study provides the first demonstration in the literature that greater use of passive coping strategies may have a negative impact on women with FHBC. The present findings also provide support for the importance of coping in determining levels of psychological functioning above and beyond that of neuroticism and extraversion. These initial results suggest the importance of additional research to better understand the role of coping styles in day-to-day affect, as well as distress specifically associated with a history of cancer in close relatives. This study makes a contribution to the broader coping literature by examining healthy women who have experienced breast cancer in their families. The findings also have implications for the development and targeting of interventions for these women. These women may benefit from individualized coping training programs designed to minimize passive coping strategies to reduce cancer-specific distress.

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